

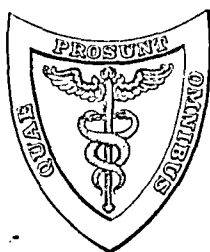


THE  
AMERICAN JOURNAL  
OF THE  
MEDICAL SCIENCES

EDITED BY  
GEORGE MORRIS PIERSOL, M.D.

NEW SERIES

VOL. CXLIV



PHILADELPHIA AND NEW YORK  
LEA & FEBIGER  
1912

44



Entered according to the Act of Congress, in the year 1912, by  
LEA & FEBIGER  
in the Office of the Librarian of Congress. All rights reserved.

# CONTENTS OF VOL. CXLIV

## ORIGINAL ARTICLES

Constipation. By DELANCEY ROCHESTER, M.D. . . . .	1
Some Clinical Observations on the Drug Treatment of Edema. By JOSEPH L. MILLER, M.D. . . . .	8
The Non-surgical Treatment of Exophthalmic Goitre. By SOLOMON SOLIS COHEN, M.D. . . . .	13
Infections Following Tonsillotomy with a Consideration of the Forms of Such Infections. By HENRY KOPLIK, M.D. . . . .	30
The Anatomy and Relations of the Tonsil in the Hardened Body, with Special Reference to the Proper Conception of the Plica Triangularis. The Principles and Practice of Tonsil Enucleation as Based Thereon. By GEORGE FETTEROLF, M.D., Sc.D. . . . .	37
Chvostek's Sign and Its Significance in Older Children. By MURRAY H. BASS, M.D. . . . .	64
A Clinical Note on Verrucæ Plantares. By RICHARD L. SUTTON, M.D. .	71
The Therapeutic Application of P-hydroxyphenylethylamin (Tyramine): An Active Principle of Ergot. By DANIEL M. HOYT, M.D. . . .	76
The Occurrence of Trichomonas Hominis in Gastric Contents with a Report of Two Cases. By FRANK SMITHIES, M.D. . . . .	82
Sacro-iliac Displacement. By JAMES K. YOUNG, M.D. . . . .	94
Hemolysis in Vivo and in Vitro as Diagnostic of Cancer. By L. W. GORHAM, M.D., and HANS LISSER, M.D. . . . .	103
A Clinical Study of a Thousand Cases of Ulcer of the Stomach and Duodenum. By JULIUS FRIEDENWALD, M.D. . . . .	157
Diarrhea of Gastric Origin: Diagnosis and Treatment. By DOUGLAS VANDERHOOF, A.M., M.D. . . . .	170
Multiple Subcutaneous Hemangiomas, Together with Multiple Lipomas, Occurring in Enormous Numbers in an Otherwise Healthy Muscular Subject. By JOHN T. BOWEN, M.D. . . . .	189
Malignant Disease of the Lung, with Special Reference to Sarcoma. By A. A. STEVENS, M.D. . . . .	193

Paroxysmal Hemoglobinuria. By ROBERT A. COOKE, M.D. . . . .	203
A Case of Delayed Development in a Boy Treated with Thymus Gland. By C. G. KERLEY, M.D., and S. P. BEEBE, M.D. . . . .	219
Acute Pancreatitis. By JOSEPH M. KING, M.D. . . . .	221
The Effect of Cold Air upon the Circulation in Healthy and Sick Individuals. By THEODORE B. BARRINGER, JR., M.D. . . . .	233
Leukocyte and Differential Counts in Ward and Open Air Treatment. By T. G. ORR, M.D. . . . .	238
Fatal Pneumothorax Following Exploratory Puncture. By HUGHES DAYTON, M.D. . . . .	241
Tuberculin Therapy in Surgical Tuberculosis. By THOMAS WOOD HASTINGS, M.D. . . . .	245
A Study of the Endocardial Lesions of Subacute Bacterial Endocarditis, with Particular Reference to Healing or Healed Lesions; with Clinical Notes. By E. LIBMAN, M.D. . . . .	313
Glomerular Lesions of Subacute Bacterial Endocarditis. By GEORGE BAEHR, M.D. . . . .	327
The Relation of Hypertension to Urinary Excretion. By CHARLES H. LAWRENCE, JR., M.D. . . . .	330
The Brain Lesions Produced by Electricity as Observed after Legal Electrocution. By EDWARD ANTHONY SPITZKA, M.D., and HENRY E. RADASCH, M.D. . . . .	341
Hospitals and Typhoid Carriers. By JOHN W. BRANNAN, M.D. . . .	347
The Therapeutic Use of Vaccines in Typhoid Fever. By JAMES G. CALLISON, M.D. . . . .	350
Stenosis of the Duodenum; a Statistical Study, with the Report of a New Case. By JAMES M. ANDERS, M.D., LL.D. . . . .	360
The Complement-fixation Test in the Differential Diagnosis of Acute and Chronic Gonococcic Arthritis. By HANS J. SCHWARTZ, M.D. . . .	369
A Critical Commentary on the Free Eye Infirmary, with Suggestions as to Reforms in Ophthalmic Hospitals, Dispensaries, and Schools. A Compilation from Correspondence and Observation. By H. V. WÜRDEMAN, M.D. . . . .	386
The Treatment of Locomotor Ataxia. By EDWARD LIVINGSTON HUNT, M.D. . . . .	398
Tuberculin Therapy in Surgical Tuberculosis. By THOMAS WOOD HASTINGS, M.D. . . . .	403
Defective Development from Arthritis in Early Life. By GEORGE DOCK, M.D. . . . .	469

The Metabolism and Successful Treatment of Chronic Joint Disease: A Preliminary Report. By RALPH PEMBERTON, M.S., M.D. . . . .	474
The Healing of Gastric and Duodenal Ulcers with Bismuth. By CHARLES D. AARON, Sc.D., M.D. . . . .	495
Contribution to the Bacteriology of Peritonitis, with Special Reference to Primary Peritonitis. By MORRIS FISHBEIN, M.D. . . . .	502
The Prognostic Significance of the Atropine Reaction in Cardiac Disease. By JAMES E. TALLEY, M.D. . . . .	514
The Therapeutic Use of Tuberculin: A Working Hypothesis and Some Personal Observations. By LAWRASON BROWN, M.D. . . . .	524
Rest Versus Climate in the Treatment of Pulmonary Tuberculosis. By WILLIAM C. VOORSANGER, M.D. . . . .	535
Diabetes Mellitus and Tuberculosis. By CHARLES M. MONTGOMERY, M.D. . . . .	543
A Further Study of the Prognostic Value of Arneth's Leukocytic Blood Picture in Pulmonary Tuberculosis, Based upon 729 Counts in 475 Patients. By PAUL H. RINGER, A.B., M.D. . . . .	561
Changes in the Kidney Resulting from Tying the Ureter. By J. F. CORBETT, M.D. . . . .	568
Clinical Manifestations of Illuminating Gas Poisoning. By ROBERT S. McCOMBS, M.D. . . . .	577
Tertiary Syphilis of the Liver. By THOMAS McCRAE, M.D., F.R.C.P. . . . .	625
Maltose in Infant Feeding. By JOHN LOVETT MORSE, A.M., M.D. . . . .	640
Bismuth Poisoning. By LOUIS M. WARFIELD, M.D. . . . .	647
Weight Curves in Typhoid Fever. By WARREN COLEMAN, M.D. . . . .	659
Observations upon Scarlet Fever, Diphtheria, and Measles at the Cincinnati Contagious Hospital. By ALBERT J. BELL, A.B., M.D. . . . .	669
Studies on the Motor Functions of the Stomach by the Use of the Gastric and Duodenal Fistulas. By THOMAS R. BROWN, M.D. . . . .	682
The More Common Forms of Cardiac Irregularity, with the Report of A Case of Heart-block. By THOMAS A. CLAYTOR, M.D. . . . .	697
Cryptogenetic Granulomatosis of the Stomach. By O. C. GRUNER, M.D., and E. J. MULLALLY, M.D. . . . .	707
The Alimentary Hypersecretion of Chronic Ulcer as Shown by the Lactose Test Meal. By DUDLEY ROBERTS, M.D. . . . .	715
Intermittent Spinal Claudication. By FRANK F. D. RECKORD, M.D. . . . .	721
The Metastasis of Hypernephroma in the Nervous System: Jacksonian Epilepsy Caused by Such Lesion. By JOSEPH COLLINS, M.D., and R. G. ARMOUR, M.D. . . . .	726

Metabolic Observations on Amyotonia Congenita. By J. G. GITTINGS, M.D., and RALPH PEMBERTON, M.S., M.D. . . . .	732
Partial Gastrectomy in a Case of Multiple Carcinoma of the Stomach. By JOHN H. GIBBON, M.D. . . . .	781
The Effects of Medicinal Doses of Aconite upon the Pulse-rate. By R. D. RUDOLF, M.D. (Edin.), F.R.C.P., and C. E. C. COLE, B.A., M.B. (Tor.) . . . . .	788
Lupus Erythematosus and Raynaud's Disease. By M. B. HARTZELL, M.D., LL.D. . . . .	793
Some Features of the Gross Anatomy of the Spinal Cord and Nerve Roots, and Their Bearing on the Symptomatology and Surgical Treatment of Spinal Disease. By CHARLES A. ELSBERG, M.D. . . . .	799
Bence-Jones Proteinuria: A Report of Four Cases with Some Chemical and Biological Notes. By THOMAS R. BOGGS, M.D., and C. G. GUTHRIE, M.D. . . . .	803
Further Experiences with the Complement-fixation Test in the Diagnosis of Gonococcus Infections of the Genito-urinary Tract in the Male and Female. By HANS J. SCHWARTZ, M.D., and ARCHIBALD McNEIL, M.D. . . . .	815
Indicanuria. By WILLIAM GERRY MORGAN, M.D. . . . .	827
Adenocarcinoma of the Thyroid, with Metastasis to the Cervical Glands and Pituitary. A Contribution to the Pathology of Abnormal Fat Formation. By D. J. MCCARTHY, M.D., and HOWARD T. KARSNER, M.D. . . . .	834
Softening of the Spinal Cord in a Syphilitic after an Injection of Salvarsan. By LEO NEWMARK, M.D. . . . .	848
Banti's Disease and Allied Conditions. By RICHARD STEIN, M.D. . . . .	856
Cases of Juvenile Psychasthenia: To Illustrate Successful Treatment. By TOM A. WILLIAMS, M.B., C.M. (Edin.) . . . . .	865
The Incidence of Purpura in the Course of Chronic Pulmonary Tuberculosis. By JOHN M. CRUCE, A.B., M.D. . . . .	875

## REVIEWS

Reviews of Books . . . . .	117, 271, 427, 585, 739, 885
----------------------------	------------------------------

---

## PROGRESS OF MEDICAL SCIENCES

Medicine . . . . .	131, 285, 439, 595, 751, 901
Surgery . . . . .	136, 291, 444, 601, 756, 906
Therapeutics . . . . .	140, 295, 449, 607, 761, 911
Pediatrics . . . . .	143, 299, 454, 765, 915
Obstetrics . . . . .	145, 302, 457, 613, 768, 918
Gynecology . . . . .	149, 305, 462, 616, 771, 922
Ophthalmology . . . . .	465
Laryngology . . . . .	152, 774
Dermatology . . . . .	308, 925
Pathology and Bacteriology . . . . .	154, 310, 467, 622, 776
Hygiene and Public Health . . . . .	619



# CONTENTS

---

## ORIGINAL ARTICLES

<b>Constipation . . . . .</b>	<b>1</b>
By DELANCEY ROCHESTER, M.D., Associate Professor of the Principles and Practice of Medicine, University of Buffalo.	
<b>Some Clinical Observations on the Drug Treatment of Edema . . . .</b>	<b>8</b>
By JOSEPH L. MILLER, M.D., Chicago.	
<b>The Non-surgical Treatment of Exophthalmic Goitre . . . . .</b>	<b>13</b>
By SOLOMON SOLIS COHEN, M.D., Professor of Clinical Medicine, Jefferson Medical College, Philadelphia.	
<b>Infections Following Tonsillotomy with a Consideration of the Forms of Such Infections . . . . .</b>	<b>30</b>
By HENRY KOPLIK, M.D., New York.	
<b>The Anatomy and Relations of the Tonsil in the Hardened Body, with Special Reference to the Proper Conception of the Plica Triangularis. The Principles and Practice of Tonsil Enucleation as Based Thereon . . . . .</b>	<b>37</b>
By GEORGE FETTEROLF, M.D., Sc.D., Assistant Professor of Anatomy in the University of Pennsylvania, Philadelphia.	
<b>Chvostek's Sign and its Significance in Older Children . . . . .</b>	<b>64</b>
By MURRAY H. BASS, M.D., Attending Physician, Children's Department, Mt. Sinai Hospital Dispensary, New York City.	
<b>A Clinical Note on Verrucæ Plantares . . . . .</b>	<b>71</b>
By RICHARD L. SUTTON, M.D., Professor of Dermatology, University of Kansas; Dermatologist to the Bell Memorial; Swedish, German, and Wesley Hospitals, Kansas City, Missouri.	
<b>The Therapeutic Application of p-Hydroxyphenylethylamin (Tyramine): An Active Principle of Ergot . . . . .</b>	<b>76</b>
By DANIEL M. HOYT, M.D., Fellow of the College of Physicians; Assistant Physician to the Philadelphia General Hospital.	
<b>The Occurrence of Trichomonas Hominis in Gastric Contents, with a Report of Two Cases . . . . .</b>	<b>82</b>
By FRANK SMITHIES, M.D., Gastro-enterologist to St. Mary's Hospital (Mayo Clinic), Rochester, Minn.	
<b>Sacro-iliac Displacement . . . . .</b>	<b>94</b>
By JAMES K. YOUNG, M.D., Associate Professor of Orthopedic Surgery, University of Pennsylvania, Philadelphia.	
<b>Hemolysis in Vivo and in Vitro as Diagnostic of Cancer . . . . .</b>	<b>103</b>
By L. W. GORHAM, M.D., and HANS LISSER, M.D., Baltimore, Md.	



## REVIEWS

Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic, Rochester, Minnesota, 1911 . . . . .	117
A Manual of Clinical Diagnosis by Means of Laboratory Methods. For Students, Hospital Physicians, and Practitioners. By Charles E. Simon, B.A., M.D. . . . .	118
The Surgical Clinics of John B. Murphy, M.D., at Mercy Hospital, Chicago, April, 1912 . . . . .	119
Lippincott's New Medical Dictionary. A Vocabulary of the Terms Used in Medicine, Dentistry, Veterinary Medicine and the Allied Sciences, with Their Pronunciation, Etymology and Signification, Including Much Collateral Information of a Descriptive and Encyclopedic Character. By Henry W. Cattell, A.M., M.D. . . . .	120
A Manual of Gynecology. By Thomas Watts Eden, M.D. . . . .	121
A Pocket Medical Formulary. By E. Quin Thornton, M.D. . . . .	124
A Handbook of Medical Diagnosis for the Use of Practitioners and Students. By J. C. Wilson, A.M., M.D. . . . .	125
Manual of the Diseases of the Eye for Students and General Practitioners. By Charles H. May, M.D. . . . .	126
Cholera and its Treatment. By Leonard Rogers, M.D., F.R.C.P., F.R.C.S., B.S., I.M.S. . . . .	127
Text-book of Ophthalmology. By Dr. Ernst Fuchs, and Alexander Duane, M.D. . . . .	127
Practical Lessons in Nursing. Fever Nursing: Designed for the Use of Professional and Other Nurses, and Especially as a Text-book for Nurses in Training. By J. C. Wilson, A.M., M.D. . . . .	129
Handbuch der Gesamten Medizinischen Anwendungen der Elektrizität Einschliesslich der Röntgenlehre. By Prof. Dr. Med. H. Boruttau, Prof. Dr. Med. L. Mann, Prof. Dr. Med. M. Levy-Dorn, and Prof. Dr. Med. P. Krause . . . . .	129
A Manual of Nursing. By Margaret Frances Donahoe . . . . .	130
Anomalie Kinder. Dr. Med. L. Scholz . . . . .	130

## PROGRESS OF MEDICAL SCIENCE

## MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

Human Infection with <i>Ascaris Mystax</i> . . . . .	131
Rigidity of Certain Back Muscles as a Sign of Pleurisy and the Frequency of Serofibrinous Pleurisies . . . . .	131
Experimental Pneumonia by Intrabronchial Insufflation . . . . .	132
Indiscriminate Drug Taking . . . . .	132
Chemotherapy of Malignant Tumors in Experimental Animals . . . . .	133
Action of Colloidal Selenium A on Cancerous Glands . . . . .	134
Urobilinuria in Pneumonia . . . . .	135
The Rectal Administration of Salvarsan . . . . .	135

**SURGERY**

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

The Surgical Treatment of Hypertrophy of the Thymus . . . . .	136
The Employment of Iodine Disinfection in the Opened Gastro-intestinal Tract . . . . .	137
Extirpation of the Gasserian Ganglion under Local Anesthesia . . . . .	137
The Experimental Production of Basedow's Disease . . . . .	138
The Use of Tincture of Iodine in the Treatment of Surgical Tuberculosis . . . . .	139
Osteomyelitis of the Long Bones . . . . .	139

**THERAPEUTICS**

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

The Treatment of Lobar Pneumonia . . . . .	140
Carbohydrate Cures in Diabetes . . . . .	140
The Treatment of Pneumonia with Camphorated Oil . . . . .	141
The Value of Inulin as a Foodstuff . . . . .	141
The Vaccine Treatment of Croupous Pneumonia . . . . .	142
The Results Obtained by Combined Sanatorium and Tuberculin Treatment of Pulmonary Tuberculosis . . . . .	142
Salvarsan Fever . . . . .	142
Acute Articular Rheumatism Treated by the Rectal Administration of Sodium Salicylate . . . . .	142
The Treatment of Chronic Cardiac Insufficiency by Intravenous Injections of Strophanthin . . . . .	143

**PEDIATRICS**

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

The Effect of Summer Heat on Infants and Children . . . . .	143
Lordotic Albuminuria . . . . .	144
Syphilitic Affections of Bones in Childhood . . . . .	145

**OBSTETRICS**

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Sepsis in the Newborn Originating in Bednar's Aphthæ . . . . .	145
The Disinfection of the Hands by Acetone Alcohol . . . . .	146
The Wassermann Reaction, with or without Treatment by Salvarsan . . . . .	147
Repeated Pregnancy after Plastic Operations upon the Tube . . . . .	148

**GYNECOLOGY**

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Vaginal Route in Bladder Operations . . . . .	149
Ovarian Tuberculosis . . . . .	150
Histologic Changes in Myomas and Ovaries after the X-rays . . . .	150
Radical Operation for Primary Carcinoma of the Vagina . . . . .	151

**DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES**

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.

Varix Involving the Soft Palate, the Left Tonsil, and the Pharyngeal Wall . . . . .	152
Retro-pharyngeal Abscess with Paralysis of the Esophagus . . . .	152
Brain Abscess, Secondary to Ethmoiditis and Frontal Sinusitis . . .	153
Ethmoidectomy for Epithelioma . . . . .	153
Carcinoma of the Rhinopharynx . . . . .	153
Laryngeal Carcinoma of Slow Evolution . . . . .	154

**PATHOLOGY AND BACTERIOLOGY**

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.

The Destruction of Red Blood Corpuscles . . . . .	154
Experimental Goitre and Cardiac Hypertrophy from Suspected Water Sources . . . . .	155
Typhoidal Bacteriemia with Localization in the Lung . . . . .	155
Antityphoidal Immunization by the Intestinal Tract . . . . .	155
The Source and Development of Generalized Tuberculosis . . . . .	156
A New Japanese Publication . . . . .	156

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

JULY, 1912

---

ORIGINAL ARTICLES

CONSTIPATION.

BY DE LANCEY ROCHESTER, M.D.,

ASSOCIATE PROFESSOR OF THE PRINCIPLES AND PRACTICE OF MEDICINE, UNIVERSITY OF BUFFALO;  
ATTENDING PHYSICIAN AT BUFFALO GENERAL HOSPITAL AND ERIE COUNTY HOSPITAL.

As the physician grows older in years and experience, he is impressed more and more with the fact that many of the disturbances of health from which people suffer are due to the neglect of the laws of health or an open violation of them. The gastrointestinal tract has been well named the *primæ viæ*: the stomach, intestines, and bowels are first in more ways than one. Besides being the first to receive the nutriment and to prepare it for anabolism, they are also the first to receive the insult of being offered for preparation not only too much material, but also that which in and of itself is deleterious, and the first to be neglected as an avenue of excretion, since many neglect the first call to evacuation and put off to a more convenient season the proper attention to that function. Neglect in childhood and early youth is the most common cause of habitual constipation. Constipation brings with it a chain of symptoms that are much more varied even than the etiological factors leading to constipation. Anorexia, nausea, vomiting, pain in the stomach, persistent and painful hyperchlorhydria, malnutrition, headache, vertigo, may be mentioned as some of the more common symptoms associated with or dependent upon constipation.

It is not, however, the object of this paper to present the many and varied symptoms which may accompany constipation, and can be classed together as the result of intestinal toxemia. I wish, instead, to cite a few cases illustrative of some of the factors in the

etiology of the condition, and, therefore, of the many different plans of treatment which have to be adopted to relieve it.

The first two cases, which I have to report, are two brothers, aged eight and six years respectively. They had both been under size when born and were brought up on cows' milk and artificial foods, neither having been nursed more than six weeks after birth. Their mother told me that they were both "naturally constipated," having had to take laxatives of some sort since early childhood.

Such a thing as natural constipation, in my opinion, does not exist. Some reason must be looked for as a cause for the deficient evacuation. In childhood such reason is found occasionally in some anatomical malformation, but this is seldom. The common cause is neglect of the habit of evacuation, or, even more commonly, a wrong diet.

When I looked over these boys I found absolutely no anatomical deformity, but on questioning the mother as to their habits and diet, I found that the custom of having stool at a special time of day had never been insisted upon, and the mother told me that she was very careful as to their diet and had always been. I was away on my vacation when consulted as to these boys, so had no means of making careful record of the physical findings, weight, urine, etc. Suffice it to say that the only abnormality found was a condition of inanition in both children. When the mother told me how she was feeding them, into the details of which it is unnecessary to enter, I was not surprised at their physical state. They were being fed on foods which had almost no residue, and they were not receiving enough even of such food.

To the joy of both boys I increased their diet considerably, giving both foods which had more food value, and what is just as important, a sufficient amount of the fodder vegetables to produce enough bulk to the residue to stimulate peristalsis. I also prescribed the amount of water to be taken daily and the times at which it should be taken. I instructed the mother to have the boys go to stool at the same time each day and try to have a passage. If this did not come without great straining, to give a small enema of soaped water to start it. I also ordered that all laxative medicines be stopped. After the third day the enema was not needed. It is over a year since this advice was given, and the boys have neither of them required a laxative since. I have several such cases on record; so I feel sure that we can put down as one of the chief etiological factors in constipation, especially in children, a lack of sufficient bulk to the residue of the food, and, as another, neglect of the habit of evacuation. The former can readily be supplied by the use of a sufficient amount of the fodder vegetables, and the latter by discipline.

The use of considerable amounts of water is also necessary. The

water is better taken chiefly between meals, but I think it is a great mistake to avoid water entirely during the meal. We should, however, insist on the thorough chewing of food before it is swallowed, and instruct our patients to be careful not to wash down half-chewed food with drink.

The following is typical of quite a large group, showing a lack of motor power and a deficiency in fluid secretion. A woman, aged about thirty-five years, gives a history of early chronic diarrhea, which had been carefully studied, showing at that time a tendency to increased motor activity of the entire intestinal tract, so that food was hurried through it in a partially digested form. This had been carefully treated at the time by diet and other appropriate remedies. Some years later she developed a tendency to constipation, which was greatly relieved by manipulation of the colon by a physician in Switzerland, who prescribed for her, when she left him, the regular use of small cannon-ball massage along the course of the colon from the cecum to the sigmoid flexure. Under this treatment, kept up night and morning, she remained in fair condition, but every now and then would have a hard, dry stool, which at times caused hemorrhoids.

In November, 1910, she came under my direct care. Careful examination of the patient showed moderate anemia of the secondary chlorotic type, coated tongue, moderate lack of appetite, slightly lowered gastric secretion, indicanuria quite pronounced, with a tendency to superacidity of urine. Her pulse and temperature were normal; she was also a little under weight. The only abnormality upon physical examination was a distinct tenderness, but no mass or muscular resistance in the right iliac region. The examination of the stool showed an abnormal dryness and a tendency to the formation of scybala. Mild laxatives produced discomfort only, but no stool. Cathartics invariably brought scybala and dry mucus; a course of bowel washes was of no lasting benefit, and massage and exercise did not give the benefit which they formerly had done. Here was a case of constipation, cecal stasis, producing congestion and tenderness of the caput coli, probably some congestion, and chronic catarrhal inflammation of the appendix, due to deficient fluid in the colon and consequently the stool was of insufficient bulk to stimulate persistalis. A considerable amount of alkaline water was prescribed, to be taken chiefly between meals, and fodder vegetables were added to the diet. Agar was given in two teaspoonful doses, twice a day, with food, and a small dose of cascara sagrada was given with each portion of the agar. The diet and general management have been kept up for eight months. The amount of agar has been gradually reduced, so that she now takes one teaspoonful as the portion. The bowels move regularly, she suffers with no gastric indigestion, the anemia

has disappeared, and the soreness and tenderness in the right iliac region can no longer be elicited even upon deep palpation.

Careful examination of the rectum should never be omitted when looking for the etiological factors in chronic constipation. Among the anatomical conditions there, which may be the chief factor or one among several, are chronic invagination of the colon into the rectum, enlargement and calcification of the rectal valves, malposition of the uterus, enlargement of the prostate gland, hemorrhoids, cicatricial stricture, pressure of a tumor on the rectum or the colon. There are many other conditions which may be found by careful examination of the rectum. I select those mentioned because they have all come under my observation in a general practice. These cases do not all come complaining of the constipation, but on inquiry the constipation and consequent auto-intoxication are the chief factors in the etiology of a large number of ailments, referred to other parts of the body.

Intestinal adhesions act not frequently as a cause of constipation.

Ptoxis of the stomach or of the colon, or both, is not infrequently present. Displacement of the colon and redundancy of the large bowel are both conditions which can be best shown by the x-rays after filling the colon with bismuth suspension.

I have two interesting cases to report illustrative of this phase of the subject.

Mrs. J. E. R. consulted me September 20, 1911, complaining of trouble with her stomach, palpitation of her heart, and persistent constipation.

Her family history was negative except that her mother had died, aged sixty-five years, of "stomach trouble."

The points of interest in her personal history are that she had had three miscarriages, at five, three, and seven months respectively, and that at the time of the last she had developed jaundice. Since that time she had had recurring attacks of nausea and occasional vomiting, and her bowels had been persistently constipated for years. She had pronounced headache, occasional dizziness, poor appetite, gastric distress after eating, cardiac palpitation, and shortness of breath on exertion. Pulse, 128, small and regular. Blood pressure, 128 mm. Hg. Temperature, 98°. She had lost forty-four pounds in the seventeen years since her attack of jaundice.

By physical examination the only abnormality in the chest was a slight dilatation of the left side of heart, allowing a mitral regurgitation; in the abdomen there was tenderness in the epigastrium, and along the left side of the abdomen, with some resistance in the left iliac region, marked tenderness posteriorly in the left lumbar region, and slight tenderness in the right hypochondrium in the region of the gall-bladder. She was sent to the hospital for further study. The study of the gastric contents and stool showed

no abnormality excepting a slight excess of mucus in each and a tendency toward hyperchlorhydria—not very marked, however.

The x-ray examination showed the stomach normal in size, shape, and position, and in peristalsis; no sign of newgrowth or obstruction.

The report on the rest of the abdomen was as follows: Cecum large and high; hepatic flexure very high and almost in the median line, thence the transverse colon dips down and rises slightly to meet the splenic flexure, which lies relatively low; the descending colon is large and tortuous as is also the sigmoid flexure. The coils of descending colon and sigmoid flexure were so large and so numerous that they undoubtedly gave rise to the feeling of resistance in the left iliac region. There were no signs of newgrowth or obstruction excepting as the unusual position, dilatation, and tortuous condition of the colon, in all its parts, especially in the descending portion and sigmoid, could produce a stagnation of the fecal contents, and so produce the obstruction to onward peristalsis.

We had here an anatomical condition which could be relieved only by exsection of a portion of the redundant colon, and this was determined upon; but the patient was in such poor general condition that it was deemed unwise to attempt any such heroic measure until her strength was built up, so three weeks were spent in a course of bowel washes, careful diet, gastric lavage when needed, and medication directed toward quieting the nervous system; no cathartics, were used, as it had been demonstrated that they did more harm than good. Under this treatment, however, no advance was made, instead she rather lost ground and was becoming discouraged.

I therefore advised that a cecostomy be performed and the colon regularly flushed from the caput coli through the anus.

After the object of this was explained to the patient, who was told that she was suffering from the absorption of toxic material from her bowel, which never emptied itself entirely, and that by this means it could be thoroughly cleansed, and that then she should be fed up so that later she could undergo the more serious operation, she gladly consented.

Accordingly on October 21, 1911, under ether anesthesia incision was made over the appendix. The colon was found very voluminous; the appendix was delivered through the wound and freed from mesentery; the wound was closed with catgut, one suture through the appendix. The skin was closed with thread. Then the appendix was tied off about two inches from the wound and fastened to a piece of gauze as anchor; the appendix was not opened.

Two days later the end of the stump was opened and a catheter introduced.

The next day the flushings were begun. All went well until



November 1, when immediately after the fluid was introduced through the catheter the patient felt badly, and soon vomited severely a large amount of fluid. It was evident that either the catheter had been pushed through the ileocecal valve or the stream had been so directed that the water was forced through and caused reverse peristalsis of the small intestine.

On November 6 and 8 the wound was enlarged by stretching with sponge tents.

The operation was performed by Dr. Roswell Park, assisted by Dr. E. R. McGuire.

From this time on the progress was rapid and uninterrupted. She went home November 28, intending to return in about six months to have the colectomy performed if it were deemed best at that time to do it.

She wrote to me under date of February 12, 1912: "I am using the irrigation regularly as you directed, the same going through every time, as it did not do at first. The opening in my side gives me some discomfort if I am walking around very much. I have not had any vomiting spells since I left the hospital. I have a good appetite and food does not distress my stomach. I am gaining in weight and getting stronger all the time and do quite a good deal of work around the house."

I think there could be no better example of the uselessness of trying to treat all cases of constipation by either laxatives or bowel washes, diet, and massage than this. Bowel washes were ineffective, cathartics worse than useless. Correction of the displacement of the bowel by massage, position, bandage and exercises impossible. So far as I can see there was but one thing to do, and that was done.

The other case in which malposition of the colon played the most important role is as follows:

Mrs. F. S., aged forty-five years, was sent to me by Dr. H. E. Battin, of Corning, on account of digestive disturbance, November 18, 1911.

Her father died of disease of the heart and her mother of chronic nephritis, each at the age of forty-six years.

She gave a history of measles, mumps, scarlet fever, diphtheria followed by arthritis, eighteen years ago, rheumatism thirteen years ago, and again three years later. Suffered with stomach trouble over twenty years ago. Has two children, aged twenty and sixteen years respectively.

Nine years ago had lacerated perineum repaired; two and a half years ago had a tumor removed from the cervix uteri. In May, 1911, the uterus was attached to the anterior abdominal wall. Menopause occurred in the preceding February.

Since the operation in May she has been troubled with digestive disturbance; very badly since July. Poor appetite, gastric dis-

tress one-half to one hour after eating; occasionally more pronounced when stomach was empty and relieved temporarily by ingestion of food; bowels have always been persistently constipated requiring laxatives every day.

The patient for the last three weeks has been on a very restricted diet and has practised gastric lavage every night four hours after last meal. Has not been benefited, and has lost considerable weight. Pulse, 64, regular, small. Blood pressure 108 mm. Hg. Temperature 98.2°. Tongue faintly coated; weight, 134 pounds; average before last May, 152 pounds. The examination of urine showed no abnormality except a marked amount of indican.

Physical examination showed no abnormality of heart, lungs, or spine, some ptosis of the stomach and colon and considerable tenderness in the epigastrium. The gastric analysis showed considerable hyperchlorhydria, some mucus, but no blood even occult; examination of stool showed no blood and rather poor digestion.

Examination by the x-rays revealed ptosis of the transverse colon with two very sharp bends at the hepatic, and splenic flexures and that the ileocecal valve was not competent; no other pathological change.

My conclusion was that she was suffering from a pronounced hyperchlorhydria, produced reflexly from the colonic stasis, the result of the displaced colon. I advised careful manipulation and massage of the abdomen for the purpose of replacing the transverse colon and emptying it; for the same purposes a daily bowel wash of 2000 c.c. of boric acid solution with the patient in the knee-chest position. I also had a properly fitting abdominal belt made for her to hold the abdominal contents in place, prescribed a diet and bismuth subcarbonate and light carbonate of magnesia to be taken as a gastric sedative after meals—no cathartics or laxatives were used, the bowels being emptied by the massage and bowel wash.

In February, 1912, in reply to a letter of inquiry, Dr. Battin wrote: "She improved markedly under the plan of treatment you outlined until December 20 when she developed acute rheumatism. She was removed to our hospital and died from uremia December 29."

The x-ray work in each of these cases was done by Dr. W. W. Plummer, to whom I wish to make acknowledgment of the value of the pictures in enabling me to establish a rational mode of procedure in treatment.

I have another case to report which is, in my experience, unique. A married woman, aged about sixty years, a *diabète gras*, had had her perineum lacerated into the rectum in early married life. It was not operated upon immediately, but subsequently three different attempts were made by most competent operators with failure to maintain union each time. How long she had

suffered from diabetes when she came under my observation I do not know, but it was for ten years at least. Under very strict diet the sugar would disappear from her urine and would stay away on a moderate starch diet for a week or two, but she would never let us see how long this period might be, for she would break into it by an excessive indulgence in chocolate candies. She had been constipated for about thirty years. She suffered from occasional headache and dizziness. She had worn glasses for a number of years, but I was not satisfied that they were correct, so I sent her to one of our most competent oculists, Dr. Elmer G. Starr. She first consulted Dr. Starr in July, 1903, and from that time for several years up into 1907. Her refractive error did not change much, but at one time while under observation Dr. Starr combined with her refractive correction a prism of 1° for right hyperphoria. The day following the first use of these glasses she had a natural movement from the bowels, and from that time on, although cathartics were occasionally required, there was no longer the necessity of the regular use of laxatives. There occurred also at that time a period of four months with absence of sugar from the urine. I report this case as an example of constipation of reflex origin, brought about and maintained by eye-strain, disappearing when this strain was relieved.

In conclusion I wish to emphasize the statements made at the beginning of this article, that chronic constipation, with resulting cecal stasis, may give rise to symptoms most diverse in character due to toxemia and sometimes to a true colon bacillus septicemia: that the causes of constipation are as diverse as, or more so than, the symptoms, and that no plan of treatment can be successful unless the etiology is thoroughly understood and the problem attacked from this standpoint.

---

## SOME CLINICAL OBSERVATIONS ON THE DRUG TREATMENT OF EDEMA.<sup>1</sup>

BY JOSEPH L. MILLER, M.D.,

CHICAGO

IN the following observations no attempt has been made to carry out extensive comparative experimental studies, regarding the action of the various agents in the treatment of edema, but rather to select a few drugs and determine, if possible, their value in different types and stages of edema. Also to note whether the

<sup>1</sup> Read before the Association of American Physicians, May 14, 1912.

failure of the individual to react to diuretics has any prognostic value.

The field of experimental therapeutics has recently furnished some interesting information upon the effect of diuretics in experimental nephritis. Animals with a mild type of nephritis respond in a normal manner to diuretics, the renal vessels dilate and there is an increased flow of urine. When, however, the renal changes are so extensive as to render the animal aneuric all diuretics fail to act. Coincident with the appearance of edema in all experimental nephritis, the renal vessels either lose their power to dilate in a normal manner, after caffein, digitalis or sodium chloride, or in case they respond in a normal manner by dilating, no diuresis results. In other words, when the kidney in nephritis reaches the point where it is unable to eliminate water, it has lost its power to respond to diuretics. This is in accord with clinical experience, as in severe cases of nephritis efforts to excite diuresis are usually futile.

Two types of cases were especially observed: Renal edema due to acute or chronic nephritis and edema chiefly cardiac in origin, in chronic interstitial nephritis. In this latter group of cases there was, as a rule, high blood pressure and these patients suffered from dyspnea, so that the effect of treatment upon this symptom would be observed. With three exceptions, the patients were hospital cases, selected because they had proved refractory to the ordinary treatment, as alkaline diuretics, caffein, sweats, catharsis, salt-free diet, and restricted liquid intake. All of these patients had been in bed for a week or more so that the effect of rest could be eliminated.

The diuretics selected were digitalis, strophanthin intravenously, theophyllin, and Fisher's solution. This latter solution was prepared by using 8 grams of crystalline sodium bicarbonate and 15 grams of sodium chloride to a liter of water.

*Chronic Interstitial Nephritis.* It is generally considered that broken compensation due to high blood pressure is one of the most unsatisfactory cardiac conditions for treatment, as it is extremely difficult to even temporarily restore compensation under such adverse conditions. A group of 8 cases of this character were given digitalis, either in the form of a tincture or digipuratum by mouth, and in 1 case, digipuratum intramuscularly. In only 1 of these 8 was there a marked diuresis; this patient received daily the digipuratum intramuscularly and reacted by a moderate increased output of urine. The average daily output of urine for three days preceding the use of the digipuratum was 860 c.c., and for the three days following its use 1400 c.c. The maximum diuresis occurred during the first twenty-four hours, when it reached 1700 c.c. gradually diminishing until on the third day it was only 1200 c.c. With this exception, the maximum daily

increase in the other patients did not exceed 200 c.c., and in the majority of cases no diuresis occurred, or it was so slight as to be questionable. In some of these patients, however, the dyspnea was considerably relieved, although there was no change in the urinary output. With a single exception all of these patients tolerated the digitalis well; one developed a marked bradycardia after even minute doses (0.08 gram daily) of digipuratum.

It was the above group of cases that showed the most striking effects following the use of theophyllin. This was administered in capsules in doses of 0.25 gram daily. On account of the nausea which usually developed, it was rarely that the drug could be continued more than three days. After a respite of a few days, the theophyllin could again be given, and by this intermittent form of treatment the edema would largely disappear. In this group of 10 cases where theophyllin was tried, 7 had previously received digitalis, with very slight, if any effect upon the edema. All of this group had interstitial nephritis with edema of the cardiac type. One patient in uremic coma had very slight edema, and was the only case in this series that failed completely to react to theophyllin. The patient died two or three days after entering the hospital. Diuresis was marked within twelve to eighteen hours after the first dose of theophyllin, reached its maximum as a rule, within forty-eight hours, and continued until the drug was stopped on account of nausea, or until the edema had largely disappeared. In the few cases where it was given continuously for a week or more, the daily output of urine grew gradually less after the first forty-eight hours until at the end of the week, when the edema had practically disappeared, the daily output was only slightly in excess of that passed previous to the administration of the theophyllin. As an example, a patient who had been passing on an average of 750 c.c. daily, had the following daily output for the six days he received the theophyllin: 1720, 2070, 2420, 1200, 1000, and 800 c.c. The average daily output of urine in the 9 cases before receiving the theophyllin was 644 c.c., and the daily average for two days following its use was 2105 c.c. The minimum diuresis was an increase from 610 to 1360 c.c.; the maximum from 630 to 3530 c.c. As a result of the lessened edema, the patients were more comfortable, although when marked dyspnea was present, this was only moderately relieved. In this respect the beneficial results were much less striking than with digitalis or strophanthin. Apparently the theophyllin had very slight beneficial effect on the heart, but acted chiefly upon the renal circulation.

During the last few months, we have injected strophanthin intravenously in 30 patients, several of these have received repeated injections. From this number 10 cases were selected in which the patients suffered from cardiac incompensation, secondary to a chronic nephritis. All of these patients were decidedly dyspneic

and had more or less extensive edema. After a single intravenous injection of  $\frac{3}{4}$  mg., there was only a very moderate diuresis. This continued, however, for several days, the edema very gradually growing less. The dyspnea was, however, very much lessened, and in this respect the action was much more satisfactory than after the use of theophyllin. Most striking was the very frequent prolonged relief after a single injection. When decided improvement was noted after a single dose, it was rarely necessary to repeat the drug until five or six days had elapsed. In several instances, by repeating the injection about once a week the patient was kept reasonably comfortable, when other forms of treatment as sweats, laxatives, and digitalis had failed to give even temporary relief. When the strophanthin was injected slowly, there was, as a rule, a moderate increase in blood pressure which in none of the cases tested exceeded 20 mm. of mercury. One patient with a very marked cyanosis, had a drop of 20 mm. in the blood pressure following the injection, no doubt due to effect on the vasomotor centre of the improved oxygenation of the blood. As a rule, no improvement was noted in the patient's condition until after a lapse of one or two hours. The intravenous injection was not followed by serious consequences except in one instance, and that in a patient with a double mitral lesion, and not included in the above series. The case had been very resistant to all forms of treatment, gradually growing worse, when as a last resort, strophanthin was injected very slowly into the vein. The patient died about twenty minutes later, and apparently the strophanthin hastened the fatal termination.

*Acute or Chronic Parenchymatous Nephritis.* Five patients with marked renal edema due to acute or chronic parenchymatous nephritis, were observed. Four of these patients had what is classed clinically as an acute exacerbation of a chronic parenchymatous nephritis; the other patient had an acute nephritis with blood pressure of 160 mm. In 3 of these patients, theophyllin failed to excite any diuresis, even after it has been continued several days. Apparently when diuresis fails to appear within forty-eight hours, it is futile to continue the theophyllin. The other 2 patients reacted by an increased urinary output, in 1 case from 350 to 1740 c.c., in the other, from 900 to 1600 c.c. Four of these 5 patients died within two weeks from the time the test was made; 1, the acute nephritis, showed marked improvement, is still living quite comfortably and almost free from edema. This patient always reacted well to the theophyllin. One patient, who in the beginning reacted well to theophyllin, later failed to respond and died in uremia. It would appear from these few observations that failure of the kidney to react to a diuretic like theophyllin indicates a very grave disturbance. Digitalis, strophanthin, and alkaline diuretics were tried in each of these patients, but without any effect. Even in the

2 patients where theophyllin excited diuresis, this was very moderate in degree as compared to that observed in the cases of cardiac edema, associated with interstitial nephritis.

Four of the patients in the above group were given Fisher's solution, prepared by dissolving 8 grams of crystalline sodium carbonate, and 15 grams of sodium chloride in 1 liter of water. Two of the patients received the solution per rectum, the other 2 by intravenous injection. Theophyllin had previously been tried in each of these cases and in only 1 was there any effect. The 2 patients taking the solution per rectum received 400 c.c. every six hours, and this was continued for two days. They had been passing from 300 to 400 c.c. daily and there was no appreciable increase during or after the treatment, nor any improvement in their conditions. Two patients were given 1000 c.c. of the solution intravenously. One of those patients had been passing on an average of 350 c.c. of urine daily. During the twenty-four hours following the injection, he passed 1120 c.c., the day following, 680 c.c., and then the previous daily output. The patient passed in the two days 1800 c.c. Previous to the treatment he had passed during the same period 700 c.c.; he received in the injection 1000 c.c. so that he only passed slightly more than the usual amount plus the quantity injected. There was no apparent improvement in the patient's condition. The second patient, receiving the intravenous injection, reacted in the same manner—the patient passing during the twenty-four hours slightly more fluid than had been introduced.

In addition to these 4 cases, Dr. Cornell at the Cook County Hospital kindly furnished me with the data of 4 cases in which the Fisher's solution was used, but the daily output of urine not measured, depending upon inspections to determine the effect on edema. During the treatment the urine of these cases was examined microscopically. The patients each received 2000 c.c. daily per rectum by the drop method for three days. Three of the patients had parenchymatous nephritis with marked edema and in each instance in addition to the casts, blood in the urine. In none of these cases was there any appreciable change in the edema. The amount of blood in the urine was, however, distinctly lessened. The fourth patient had apparently an interstitial nephritis, cardiac asthma, scant urine, and very slight edema. After the Fisher's solution had been given for two days, the edema became so marked that it was necessary to discontinue its use.

These observations do not add anything to our knowledge of nephritis, but merely emphasize certain well-established facts. When the permeability of the kidney to fluids, in nephritis is seriously impaired, it is difficult and often impossible to restore this function by any measures at our command. Edema of cardiac origin, even when secondary to nephritis, may often be at least temporarily relieved by diuretics or cardiac tonics.

## THE NON-SURGICAL TREATMENT OF EXOPHTHALMIC GOITRE.<sup>1</sup>

By SOLOMON SOLIS COHEN, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JEFFERSON MEDICAL COLLEGE; PHYSICIAN TO THE  
PHILADELPHIA GENERAL HOSPITAL, ETC., PHILADELPHIA.

GRAVES' SYNDROME NOT HYPERTHYROIDISM ONLY. The pathogenesis and pathology of Graves' syndrome are as yet obscure. "Hyperthyroidism," despite its present currency, is a faulty, as well as an insufficient, explanation. Excessive activity of the thyroid gland, sometimes accompanied with goitre and sometimes without appreciable enlargement, is often present and adds its symptomatology to that of the underlying disorder; but it is neither the origin nor the whole expression of the fundamental departure from the normal. The term "exophthalmic goitre" is unfortunate; and probably leads to belated diagnosis; early stages being overlooked, or mistaken for "nervousness," gastro-enteric disorder, etc. Luckily, "neurasthenia" and "hysteria" are often treated by rest.

OPERATIVE TREATMENT UNNECESSARY IN THE MAJORITY OF CASES. Holding the view set forth, I am unable to look upon Graves' disorder as essentially a condition for operative treatment; or to admit that the only alternative is cytólisis. That partial thyroidectomy, ligation of the thyroid arteries, and other approved surgical procedures are helpful in many cases and necessary in some, may be freely granted; and one may likewise acknowledge without reserve the great value of Beebe's serum in certain cases. Yet I have a strong conviction, based on more than twenty-five years' observation and study, that such measures are indicated only in a small minority of the cases that come under the eye of the alert physician.

INDICATIONS FOR OPERATION. Whether or not operation is indicated in an individual case, is to be decided upon the special circumstances of that case; and these cannot always be set forth categorically. Nevertheless there are certain general considerations that may assist the decision. Thus there can be little question that operation should be done:

1. When the disorder has persisted for a long time, and is advancing despite skilful medicinal and hygienic management, including prolonged rest.

2. When the disorder is progressive or far advanced, and is either disabling or dangerous, or threatens to become so—even though no sufficient attempt has been made at medicinal and hygienic management, including rest.

<sup>1</sup> An address delivered before the Medical Society of the State of New York, at Albany, April 17, 1912.



3. When the patient's means or social status is such that rest is impracticable, and the disorder, although slight, is partially disabling and has persisted for a year or more under treatment, with no sign of yielding.

There are other circumstances, however, which need not be enumerated, in which the decision is not so easy. Usually no harm will be done in such doubtful cases by waiting and watching for a reasonable time, giving the patient meanwhile the benefit of rest and other appropriate measures. In a proportion, even of advanced or apparently progressive cases, arrest or partial recovery will take place to a degree sufficient to obviate the necessity for surgery.

While, therefore, avoiding an extreme position against the operative treatment of Graves' disorder, and on the contrary recognizing its necessity and its benefits in properly selected cases, I am, nevertheless, distinctly and unalterably opposed to the dictum that operative treatment is the sole means of remedy in any case, and should be the rule in all.

FALLACY UNDERLYING ARGUMENT FOR ROUTINE SURGERY. Underlying most of the arguments for making operative treatment the rule, is the false assumption that without such interference recovery cannot take place. On the contrary, the great difficulty acknowledged by most of those who have had large experience in the medicinal management of Graves' syndrome is the liability to overestimate the influence of some particular therapeutic measure, during the use of which the patient may have recovered spontaneously. For it must be remembered—and in connection with the claims of surgeons as well as with the assertions of physicians—that in a very large number of cases recovery will take place without any special method of mechanical or medicinal treatment, if only the patient be kept at rest, with regulation of diet, and under proper hygienic surroundings, *for a sufficient length of time*. Indeed, spontaneous recovery may occur, even without prolonged rest. This, however, is less common.

DANGERS FROM THE GOITRE. Let me repeat that I do not wish to be misunderstood as opposing operation under all circumstances. When the diagnosis has been unduly delayed, or when the hygienic and medicinal management has been faulty—and faulty chiefly by the failure to institute persistent rest—the thyroid complication may in consequence become the predominant factor in the case. Pressure by the enlarged gland may cause mechanical difficulties in respiration or in deglutition; may obstruct circulation in the cervical vessels; or by compromising the pneumogastric or other nerves, may give rise to disorders of various kinds. Also, by excessive activity, the hypertrophied gland may disturb cardiac and other functions in great degree. In such instances surgery may indeed be the only remedy; or, as already intimated, it may be the remedy of preference; and it is quite probable that many surgeons, and

especially those noted for their skill in thyroid operations, have formed their opinions concerning the nature and management of exophthalmic goitre in general, largely upon cases of this class. These are, nevertheless, but a small minority of the whole.

APPROXIMATE ESTIMATE OF SURGICAL AND NON-SURGICAL CASES, AND CASES OF SPONTANEOUS RECOVERY. I have no exact statistical data, but as a guess, not without reasonable grounds, 20 per cent. of all the cases of Graves' disorder may be looked upon as a rather large estimate of those belonging to this category of neglected cases. Again, there are cases in which the diagnosis is made reasonably early and the medical management, including rest, has been reasonably thorough, yet which nevertheless progress to a point at which surgical interference becomes necessary. If one may judge from his own experience, 5 per cent. would be a very large estimate for this category. Thus we have left, as a conservative estimate, about 75 per cent. of all the cases to form the great class in which recovery may be expected spontaneously or under non-surgical treatment. Of these, probably 50 per cent. will recover without special medication. In the remaining 50 per cent., that is to say, somewhere between 30 and 40 per cent. of all the cases of Graves' syndrome, careful medical management is necessary; and if skilful and persistent, will be successful.

GENERAL CONSIDERATIONS UNDERLYING THERAPY. Before taking up the details of such management it is necessary to consider briefly certain general questions. Therapeutics would be more direct and less empirical if we had more definite information concerning the actual etiology of the condition.

Unquestionably there are three factors in its causation, perhaps more. These three certain factors are: (1) A fundamental liability; (2) a provocative agent; (3) a local determinant.

1. The underlying fundamental liability is congenital, and usually hereditary. It predisposes not merely to exophthalmic goitre, but to disturbances of the autonomic nervous system in general. I have discussed this at length in many papers,<sup>2</sup> referring to various forms of vasomotor and visceral disorders, and need not here elaborate.

2. There must be, however, a provoking agent; and this is not always the same. Psychic disturbances—and usually emotion of a depressing character, such as grief, anxiety, fear or fright, but sometimes of an exciting order, as anger—undoubtedly acts as a provocative in many instances, though it cannot always be traced when the patient comes under observation. It is possible that emotion acts indirectly through the generation of toxic substances.

<sup>2</sup> Vasomotor Ataxia: AMER. JOUR. MED. SCI., February, 1894; Trans. Assoc. Amer. Phys., 1902; and Medical Review of Reviews, January, 1912. Visceral Angioneuroses: Trans. Assoc. Amer. Phys., 1909; New York Med. Jour., February 19, 26, March 5, 1910, Graves' Syndrome, Raynaud's Syndrome, and Allied Disorders: International Clinics, 1909, vol. iii, S. 19.

Be this as it may, toxic influences of various kinds apparently play a large part in the complex etiology. Their nature, however, is as yet highly obscure, and little is to be gained by enumerating the many guesses that have been put forward concerning intestinal toxins, bacterial toxins, the products of perverted metabolism, anaphylactic products, deranged internal secretions, etc., since the evidence is inconclusive, and, moreover, the correctness of one supposition does not exclude the possibility of the others being right also. Beyond doubt the etiology is multiple.

3. The local determinants are probably many, but they are also as yet unidentified. Suggestive are the variations in the size of the thyroid gland brought about by pregnancy, by parturition, by lactation, by ovulation, by menstruation, or by the failure or excess of some of the special functions of the female, and under sexual excitement in both male and female. I have observed in the immune members of tuberculous families, and in persons exhibiting very sluggish or very rapid tuberculosis, various autonomic disturbances, including thyroid enlargement and ocular symptoms; and the tendency of some cases of Graves' disorder to terminate in pulmonary or general tuberculosis is recognized. So, too, the occurrence of exophthalmic goitre in members of neurotic families, and the development of maniacal excitement and other forms of psychosis in a certain proportion of the patients, is well known. Glycosuria may be an accompaniment of Graves' syndrome, and in some instances diabetes mellitus may be the terminal manifestation. Here the reciprocal relations of pancreas and thyroid, or of both to the pituitary and nervous centres, may be involved.

Whether eye-strain is to be classed as a provocative or determinant, or both—or whether the changes in the refractive apparatus and the disorders of muscle and innervation are not, rather, collateral results of the more fundamental cause—cannot be dogmatically stated. Probably there is a "vicious circle."

Without enlarging further on this difficult problem, it is evident that the exciting factors are both multiple and obscure, and that any treatment that attempts to base itself upon an unvarying etiology must fail in a large number of cases.

**THERAPEUTIC CLASSIFICATION.** From a therapeutic standpoint it would be highly desirable, if possible, to classify our cases etiologically or pathologically, and analyze the results of treatment accordingly; but as yet we lack the basic data. So, too, clinical classification fails for a similar reason; that based upon the varying characteristics of the goitre being useful, but inadequate. A rough clinical division may be made by noting the order of development, or the relative severity, of the cardinal symptoms. There are cases in which the cardiac disturbance appears long before enlargement of the thyroid can be demonstrated; cases in which the thyroid enlargement is first noticed; and cases in which the ocular

manifestations precede all others, though these last are rare. Again, there are cases in which cardiac disturbance, or thyroid enlargement, or exophthalmos are relatively slight or completely wanting; and cases in which one or the other of these symptoms overshadows all else. There are cases of apparently abrupt onset, and cases of slow and even insidious onset. There are cases in which the early symptoms are predominantly nervous; others in which visceral functions, especially of the digestive or respiratory apparatus, are most prominent. Each physician doubtless makes some such classification of his own patients, and governs his treatment, in a measure, accordingly. But there is no accepted classification satisfactory to all; and there cannot be until etiology and pathology are cleared up.

One feature of a possible clinical classification is, however, of much significance. That thyroid enlargement may be wanting throughout the whole progress of the case is attested by many observers. It has been my own fortune to observe and record a number of such instances. Those in which thyroid enlargement is slight, and sometimes intermittent or variable, are still more numerous; and those in which goitre is quite a late symptom form a considerable proportion, perhaps one-fifth, of the whole number of cases. Certainly in that group of cases in which thyroid enlargement is wanting, slight, or delayed, medicinal rather than surgical treatment is indicated.

RECOVERY—WHAT IS IT? This leads directly to another very fundamental question: What constitutes recovery? Until this is settled, it is impossible to give judgment not only as to the comparative merits of medical and surgical management, but also upon the relative merits or absolute effects of the various medicinal measures and surgical procedures suggested. If disappearance of thyroid enlargement is to be taken as the criterion of recovery, then those patients in whom there has never been such enlargement, can never be said to have recovered, despite the loss of all other symptoms—an evident *reductio ad absurdum*. But if in cases without thyroid enlargement recovery must be predicated upon the subsidence of cardiac and nervous disturbances, may not the same rule be fairly followed in cases in which similar disappearance of cardiac and nervous disturbances takes place, but thyroid enlargement remains? And what shall we say concerning patients who no longer have goitre, but in whom all the other phenomena of Graves' disorder persist? And just what degree of reduction in exophthalmos is to permit the case to enter the list of recoveries, or what degree of persistence is to exclude it?

It so happened last fall that I was able to exhibit in one of my clinical lectures at Jefferson Hospital, two patients side by side. One was a girl who had had all the symptoms of pronounced Graves' disorder. Her heart and eyes were now practically normal;

she had no tremor; she could sleep well; she had gained flesh, and indeed seemed in every respect restored to full functional health; but there still persisted a moderate enlargement of the thyroid gland. This girl walked into the clinic hall, and had been up and about her work for more than a year. The other patient was a man who had to be rolled into the arena in bed. He was emaciated; he still showed marked exophthalmos, almost continuous tremor of the hands, and tumultuous heart action; his face was continuously flushed; he was subject to fits of sweating, to insomnia, to gastro-enteric crises, to headache, and to violent nervous excitement; but he had no goitre. His thyroid gland had been removed thoroughly and skilfully about two years before he came into Jefferson Hospital by a western surgeon of high repute (let me add in parenthesis, not at Rochester). The parathyroids had probably been taken with it, for there was a history suggestive of mild tetany following the operation. Which of these two patients could be the more appropriately said to have recovered?

Mere survival after operation is not recovery!

The condition of the thyroidectomized patient described is not to be attributed to the completeness of the operation, for his symptoms were not those of *cachexia strumipriva*—of myxedema—but of Graves' disorder; of miscalled "hyperthyroidism." Someone may guess that he possessed overexcited supplementary thyroids, but that supposition need not be argued. His goitre was gone, but all that was essential in Graves' syndrome remained.

When a partial thyroidectomy is done, the condition of the patient with respect to the thyroid gland is not materially different from that of a patient whose thyroid gland has become reduced, although not to normal size, under non-surgical measures. Judging from the patients and photographs that I have seen, complete restoration of the eyes to normal, after any marked degree of exophthalmos, is exceptional. Material correction of ocular symptoms seems as frequent under non-surgical measures as after operation. It is therefore to the nutrition, and to the cardiac and nervous disturbances—including visceral disorders—that we must first look in order to determine the effect of treatment. Concerning the goitre and the exophthalmos we must require these to have so far subsided as to be neither dangerous nor disabling, but that is all. We are not discussing the merits of either surgical or non-surgical management from a merely cosmetic viewpoint. As a matter of fact, however, there is rarely left any marked deformity of the eyes or of the neck, when the essential—that is to say the neurocardiovascular or autonomic—symptoms of Graves' disorder have been overcome.

ULTIMATE RESULTS. Recovery has to do, however, not only with the immediate result of treatment, whether surgical or medical, but with the patient's ultimate fate. This is not always easy to

ascertain, especially with the large number of patients seen in hospitals. In Volume LXV (1911) of *Guy's Hospital Reports*, Dr. Hale White records the result of an attempt upon his part to trace the history of patients discharged after medical management during the last twenty years, and he finds that in above 80 per cent., the recovery has been permanent. Postoperative statistics of equal length are not at hand; but such reports as are available concerning the ultimate fate of patients submitted to operation and recovering therefrom are, at all events, no better than this. In my own personal and consultation practice I have had the opportunity to observe, directly or through the attending physician, a number of patients for periods of from a few months to twenty-five years after apparent recovery under non-surgical treatment. In but one instance has there been relapse, and in no case has death occurred from any condition with which Graves' disorder could be causatively associated. Among these cases, however, those of patients who have remained under prolonged, continuous observation are relatively few (somewhere between 25 and 30) and form but a small proportion of the whole number of cases treated in hospital and private practice. The attempt to trace out a sufficient number of the others upon which to base a statistical report of any special value has thus far failed. I have, however, numerous records of patients (approximately 100), in whom recovery had endured for periods varying from three to five years before touch with them was completely lost; and if in a matter of such importance one may speak of general impressions, I am inclined to believe that Dr. Hale White's result will represent pretty closely the general experience.

Since, then, under medical management one may reasonably hope for the recovery of not less than 75 per cent. of patients exhibiting Graves' syndrome; and since it is to be fairly expected that the recovery will be permanent in at least 80 per cent. of these, one is more than justified—he is bound—to give his patient the opportunity to recover without the risk and danger of operation and operative sequelæ; exception being made of those cases already alluded to, in which the size or characteristics of the tumor, the rapid advance in severity of symptoms despite proper medicinal management, or the circumstances and environment of the patient render immediate surgery necessary.

**ELEMENTS OF MEDICINAL TREATMENT; REST.** What then constitutes "proper" medicinal treatment? (1) Rest, (2) *rest*, (3) **REST**. This is the most important factor of all, especially in cases which have so far advanced as to exhibit a thyroid enlargement that may properly be denominated goitre; or in which, although goitre may be slight or absent, there is a decided tendency to loss of flesh and strength. There are, however, degrees and kinds of rest; and one must adapt this measure, as all others, to the symptoms of the individual case and to the personal peculiarities of the patient.

Relief from worryment and other forms of mental disturbance, as well as from eye-strain and other sources of reflex irritation, forms an integral portion of the rest treatment. In arranging its details, the nutritional, cardiac, and nervous phenomena should be given the greatest weight—not only in determining whether the patient is to be kept at absolute rest for the twenty-four hours, or allowed a certain degree of movement for limited times, but also in fixing the period over which the treatment is to be prolonged, its modifications from time to time, its intermission and its resumption, as well as the necessity for adding to it other therapeutic measures.

**AIR, FOOD, WATER.** It is almost needless to say that the rest must be combined with regulation of diet, and that due care must be paid to the ventilation of the sick room, to cleanliness, to the sufficiency of the secretions and excretions, and to all other points of good nursing. A word or two, however, may be ventured concerning air, food, and water from another viewpoint.

Whether or not I am correct in the supposition that there is a curious (so to say, *inverse*) fundamental relation between Graves' syndrome and tuberculosis—namely, that one may appear instead of the other in different families of a common stock, in different generations of one family, or in different members of one household; and whether or not this has anything to do with the curative virtue of iodine in early tuberculosis and the specific function of the thyroid gland as an iodine accumulator—at all events, the diet and regime useful in tuberculosis will often be found correspondingly useful in Graves' disorder. Rest in the open air continuously, or for a large portion of the time, is superior to continuous indoor rest, albeit in the best ventilated room, in either instance. In my own experience, patients with pulmonary tuberculosis or intestinal tuberculosis do best on a diet consisting largely of raw or underdone broiled or roast beef and hot water; and I have found the same regime useful in many cases of Graves' disorder.

The hot water is sufficiently important to be emphasized by repetition. Given regularly and in sufficient amount, *i. e.*, from 250 to 500 c.c. (one or two tumblerfuls) and preferably the larger quantity, about an hour before food four times daily, and between meals also, *ad libitum*, it keeps the gastro-enteric tract clean and active; and it promotes elimination by the skin, the bowel, and the kidneys. Thus it permits a sufficient quantity of beef to be eaten, digested, and assimilated; and causes the waste products to be excreted thoroughly.

In both Graves' disorder and tuberculosis there is a distinct failure in the digestion and utilization of carbohydrates, and in both conditions patients do well on a minimum of sugars and starches. In both, there seems to be the necessity for the administration of a sufficiency—the amount varying with the individual—of green vegetables and fresh fruits. By green vegetables I mean lettuce,

celery, spinach, water cress, and the like; leaves, stems, and fruit, rather than roots and tubers. In both conditions not only sweets, but salty things and certain vegetable acids seem to be injurious; hence the patient must eschew candy, cakes, pastry, etc., as well as pickles, chow-chow, salads made with vinegar, tomatoes, and the like. The necessity to prohibit an excess of vegetable acids does not, however, imply the exclusion of citrus fruits in moderation; these are, as a rule, beneficial. Concerning milk and eggs, while their value as a special regime has been much exaggerated, they may be utilized judiciously. In fact, in some cases, during the first prolonged period of rest, milk will have to form the staple of diet. It should be given heated or predigested, or both, and not in excessive quantity. Too many egg yolks are not desirable, and some patients cannot take eggs at all. It is true that milk and eggs given to a patient taken from the slums and exhausting work and placed at rest under sanatorium conditions will bring about at first a large gain in weight, but the gain rarely holds when the patient returns to ordinary life, even under improved conditions. The gain that is made upon a beef diet is not so rapid, but it is more lasting.

There are, however, certain patients with Graves' disorder who cannot tolerate either an exclusive diet of beef, or even a large proportion of meat in an otherwise varied dietary. In such cases the necessary modifications must be made. The word "idiosyncrasy," it must be admitted, is a too convenient cloak for ignorance; yet in the absence of a better term, or rather, of better knowledge of the condition indicated, we are compelled to use it. It can therefore be said in summing up the question of diet, that patients with Graves' syndrome exhibit many idiosyncrasies in this respect. "One man's meat is another man's poison" here, to greater degree than in any other condition with which I am familiar. The physician must take the time and the pains to learn the "meat" and the "poison" of each individual patient; for there can be no doubt that toxic products of various kinds, alimentary and metabolic, play a large part in inducing or aggravating many of the Graves' phenomena, altogether apart from the direct influence of diet upon gastro-enteric disturbances.

**INDIVIDUALIZATION IN HYDROTHERAPY.** Individualization, indeed, is the keynote throughout the treatment; not only as regards rest and diet, but as to all other measures also; including those of hydrotherapy, to which we may now give brief attention. Whether or not the view is correct, that as regards the production of the symptoms consisting the syndrome group described by Graves, as in various allied disorders, the autonomic nervous system, and especially the taxic mechanism of the cardiovascular apparatus, is primarily at fault, experience proves that one of the most potent influences in controlling these symptoms is re-education of the vasomotor taxis, peripheral and central, by alternate hot and cold applications to



the surface of the body. There are many ways of doing this. The simplest, and in the case of patients under absolute rest treatment, the best method, is, after a preliminary cooling of the head and neck, to sponge the entire body rapidly with water as hot as can well be borne (in the neighborhood of  $108^{\circ}$  to  $112^{\circ}$  F.), and to follow this immediately by what is called a "cold friction rub" with water cold as can well be borne; which may at first be only  $80^{\circ}$  or  $70^{\circ}$  F., as but later as low as  $60^{\circ}$  or  $50^{\circ}$  F., or, in rare instances, even ice water. The whole process, including the final drying with a rough towel, should not take longer than from five to eight minutes. Here again, however, there are numerous modifications to suit the individual condition and the individual reaction. Also, in the progress of the case, the time and the temperature, and the method of the applications must be adapted to their effect on the one hand, and to the new conditions on the other. Hot and cold packs, sprays, dcuches, momentary plunges, and the like, are also applicable; the details being modified, of course, by common sense. It is well to instruct the patient to continue the hot and cold sponging or spraying throughout life; to make it a part of the morning toilet, altogether independent of the ablutions of mere cleanliness.

**MASSAGE AND MANIPULATIONS.** In the absence of fever, certain mechanical measures, as light massage, intermittent pressure upon the muscular masses along the spine, and other expedients for exciting spinal-autonomic reflexes, as the concussion or sinusoidalization of Abrams, may be useful. One must be guided largely by their effect upon the circulation, especially pulse frequency, blood pressure, and subjective sensations of heat and cold. Details cannot here be discussed.

**PREPARATIONS OF DUCTLESS GLANDS.** The therapeutic utilization of various preparations of animal tissues, and especially of the ductless glands, finds a peculiarly appropriate field in Graves' disorder. Nevertheless frequent disappointments must be looked for. The difficulties are two: (1) To choose the particular agent most appropriate to the individual case; (2) to procure a trustworthy preparation. It is to be regretted that many of the commercial preparations are uncertain, and some of them inert. This was long ago borne in upon me, not only by the difference in result in cases apparently alike in essential particulars, under what was meant to be the same treatment, but also by the variation of effect in individual cases, with different preparations of the same agent. A fresh liquid extract in glycerin or other proper menstruum, administered by intramuscular injection, or if the menstruum be suitable, by intravenous injection, is, in my own experience, the most potent. Feeding the fresh raw tissue is also efficacious; but apart from the difficulty of obtaining it, there are few patients who will persist in eating the raw substance in sufficient quantity and for a sufficient length of time. The desiccated powders and tablets upon the market

vary in efficacy with their source, as well as their freshness, and this there is no means of determining. Moreover, they commonly contain, together with the active principle desired, more or less putrid, or putrescent, or potentially putrescent, animal matter, which is quite likely to cause gastro-enteric disturbance, if nothing more.

With all these drawbacks, however, it is sometimes possible to bring about considerable improvement, even by the administration of the commercial powders, if care be taken to specify the products of manufacturing pharmacists worthy of confidence. There are also obtainable some good liquid preparations suitable for injection. The treatment to be successful must be persistent. Miracles are not to be looked for.

On the whole, *thymus gland* is the most useful of the ductless gland preparations in the largest number of cases. It must be given in sufficient quantity—from 0.5 to 3 grams (8 to 45 grains) of a good commercial desiccate or the equivalent in other forms—daily, for months together. I still, however, find, as reported to the American Medical Association<sup>3</sup> fifteen years ago, the conjoint or alternate use of *adrenal* and thymus preparations, even better.

More recently I have been making observations with *pituitary* preparations. While the whole gland is useful, there is reason to believe that a certain antagonism exists between the anterior and posterior portions, and that the latter is the effective agent. I have not been able to observe any material difference between the therapeutic effect of the pars intermedia alone, and that of the whole posterior lobe (including the intermedia and the nervosa); and the whole posterior lobe is easier to obtain and cheaper. One of the earlier patients to receive pituitrin injections was a woman at the Philadelphia General Hospital who had been in the house for more than two years before she was brought to my personal attention, and who had during that period been under the care, from time to time, of several of my colleagues, as well as of one of my assistants. She had been treated in various ways, but chiefly as the Frenchman advised that coryza should be treated—"with contempt." Surgery had been proposed and declined. There had been ample time for spontaneous recovery, if it were to occur. The case was one of moderate severity, with periods of extreme tachycardia, and the exophthalmos was of such degree that about one-fourth of the eyeball was left uncovered when the attempt was made to close the lids. Intramuscular injections of pituitrin, at first in small (*circa* 5 minims, 0.3 c.c.), and afterward in rather large doses (20 to 30 minims, 1 to 2 c.c.) were given, at first once, and afterward thrice, daily. Improvement, both subjective and objective, was marked and rapid. Soon it became impossible to keep the patient in bed; and I was unable to exhibit her to the Philadelphia County Medical Society as arranged for, because a change in the date of some of

<sup>3</sup> Jour. Amer. Med. Assoc., July 10, 1897.

the Society's work having caused postponement for a month, she refused to remain longer in the hospital, and afterward could not be traced. The heart had become quiet, the goitre was scarcely more than visible, and the eyelids closed almost completely. Such rapid and remarkable improvement is not the rule. The effect is gradual, but progressive, and the pituitary needs to be supplemented by thymus or other appropriate adjuvant.

Concerning the *theory* of treatment with ductless-gland preparations, so much could be said, and yet with so little certainty, that it is hardly worth while going into the subject here. Even should one master all the facts contained in Sajous's great work, he would not arrive at assurance concerning the interrelations of the hormones and hormonogenic tissues, but merely at a more comprehensive view of his ignorance. The rationale of organotherapy, or if the term be preferred, hormonotherapy, in Graves' disorder, is doubtless different in different cases. In some, a toxic agent—which may be merely an excess, or perhaps a perversion, of a normal secretion; or may be an excretion product abnormally retained; or may be a wholly abnormal substance—is inhibited, neutralized, or otherwise counteracted. In other instances, the product employed medicinally acts as an exciting agent, stimulating deficient normal activity—perhaps of an antagonizing gland. In others, it complements or supplements or replaces the action of normal or deficient organs or secretions. Thus the ultimate effect may be (directly) that of the tissue or organ administered, or (indirectly) that of some other tissue or organ which it arouses; or the entire action may be merely inhibitory. The somewhat contradictory pathology of the thymus gland aptly illustrates this fact. It is found abnormally persistent or enlarged in some cases of Graves' disorder; but also sometimes in myxedema, and frequently in acromegaly. We cannot yet dogmatize concerning the natural complementations and antagonisms which doubtless we avail ourselves of, in the administration of the organ-preparations. And as, furthermore, we have at present no means of ascertaining clinically just what is needed in any special instance, we are compelled in most cases to resort to the therapeutic test itself, by tentative administration of the various agents, before we can determine which is best for the particular individual under treatment.

The great drawback to this sort of empirical choice is the fact that a few days does not suffice to make the test; a month or more may be required. Notwithstanding this, it is worth while; and, as one accumulates experience, he begins to formulate for himself certain *indications* that guide in the tentative selection, and most frequently guide aright. One such indication, upon which the use of the pituitary preparations or of epinephrin (the adrenal principle) may be based, is the systolic blood pressure. When this is

especially low, say less than 100 mm. Hg., one of these substances should always be administered, whether or not thymus is given coincidentally. If pulse frequency diminishes and systolic pressure increases more than rest alone can account for, then one may be sure that he is on the right track.

Among other organic preparations that are sometimes useful, is *extract of spleen*, as in a remarkable case reported by H. C. Wood; but I have no personal experience with it. It is a curious fact that *thyroid gland* is remedial in some cases, even in patients with marked goitre and without myxedematous or other symptoms indicative of thyroid atrophy. One such instance, in a man under my care at the Philadelphia General Hospital some twenty years ago, I have reported. In this case there were marked exophthalmos, continuous tremor, fits of cardiac palpitation, and many and various nervous symptoms. Goitre had been present, but the thyroid, at the time I saw the patient, was not markedly enlarged. This might indicate, of course, a beginning atrophy. But, on the other hand, there are cases with incipient Graves' phenomena—*formes frustres* and others—but with little or no thyroid enlargement (or with intermittent thyroid enlargement) also benefited by thyroid substance; a fact suggesting the existence of a class of cases in which over-activity of the thyroid is at first a defensive reaction, only later becoming, by its excess, offensive. The medicinal use of thyroid substance permits the gland to become quiescent, and obviates the later pathological phenomena. Such treatment, however, is to be undertaken tentatively and cautiously; for in the ordinary case thyroid is harmful. Its administration should, indeed, be avoided altogether by those who have not had large experience, not only with Graves' disorder, but also with the use of thyroid preparations in various other conditions.

*Parathyroid extract* is useful in many cases, especially in controlling tremor and allied nervous symptoms. I frequently conjoin its use with that of the thymus, adrenal or pituitary preparations. Large doses are not necessary. From  $\frac{1}{10}$  to  $\frac{1}{2}$  grain (5 to 25 mg.) of the desiccated commercial preparation, given thrice daily for limited and recurrent periods, usually suffices. Its effect seems to be enhanced by the concurrent administration of a calcium salt, and this latter may be given with food, if necessary, replacing table salt. It is possible and plausible that the tremor is indeed due to compromising of the parathyroid glands in the course of the pathological process.

Not only in the administration of parathyroid substance, but also in the use of the other glands, it is well to intermit and alternate; replacing thymus, for example, with adrenal or pituitary; or using in place of adrenal one of the mineral or vegetable drugs of similar pressor effect. One reason for this is that the antigen action of the animal products is a factor to be reckoned with. This is not

theoretical only; in some of my cases, antibodies (to pituitary substance) have been demonstrated in the blood (by Drs. S. D. W. Ludlum and Ellen T. Corson-White). The antigenic effect is a double-edged sword, cutting both ways, and it complicates the therapeutic problem still further. I have never attempted to inject thyroid extract in minute quantities as an antigen—a vaccine—but it is not impossible that some such procedure might be worked out, and be useful so far as concerns mere hyperthyroidism.

The well-known connection of menstrual disorders with Graves' syndrome has suggested the use of *ovarian substance* and *mammary gland substance* to control special symptoms. I have seen no benefit from either. Incomplete observations with lutein (from the *corpus luteum*) are, however, more promising; but as yet nothing definite can be said.

**INTESTINAL ANTISEPSIS.** *Intestinal antiseptics* appear to be useful auxiliaries to treatment. Whether or not the disorder is originated by the absorption of toxic products from the intestine, it is certainly aggravated thereby. Dieting does much to diminish this liability. In addition, however, it is well to wash out the colon thoroughly with hot saline solution once or twice weekly, and to administer such agents as the salicylic compounds, beta naphthol, benzonaphthol, hexamethylenamin, guaiacol carbonate, and the like, singly or in association, from time to time. Also an occasional course of calomel, followed by a saline aperient, or the occasional use of castor oil, and the cholagogue purgatives, helps.

*Menthol* has been urged as a specific. Whether it acts as an intestinal antiseptic or otherwise, some cases are greatly benefited by it. I was first led to its use by the history of an intelligent patient presenting other symptoms of vascular disorder, but in whom I could not find enlargement of the thyroid gland or exophthalmos. Observing me search for these signs, the man informed me that he had had exophthalmic goitre some ten years previously, but had recovered while taking menthol. That may have been a coincidence, of course; but at all events the drug is useful in some cases; and it may be tried when other means have proved inefficacious, or as a succedaneum to the organ-preparations during the periods of intermission.

**SYMPTOMATIC MEASURES.** In addition to the general treatment of rest, fresh air and dieting, hot and cold applications, intestinal antiseptics, and the administration of organic extracts, there are various measures, medicinal and physiological, that may be useful in controlling or mitigating symptoms. Since these are familiar to most, they may be mentioned briefly.

For the nervous erethism, especially if there is a tendency to insomnia, *strontium bromide* in doses of from 2 to 4 grams (30 to 60 grains) twice or thrice daily, according to circumstances, may be given. *Hyoscine hydrobromide*, or, better, *Scopolamine*

*hydrobromide*,  $\frac{1}{4}$  milligram ( $\frac{1}{250}$  grain) or less, once or twice daily, is helpful. The treatment suggested by Forchheimer, namely, *neutral quinine hydrobromide*, 5 grains or more thrice daily, is also of considerable service in controlling the cardiac and nervous symptoms. I have sometimes observed even better results when *ergot* and *picrotoxin* are associated with the quinine salt, than when it is given alone. When there is considerable tendency to erythema, purpura, urticaria, and similar angioneurotic phenomena, these same drugs (neutral quinine hydrobromide, ergot, and picrotoxin) are also useful, and may be given singly or in conjunction, according to the effect in the particular case. *Hydrated calcium chloride*, calcium lactophosphate, calcium glycerophosphate, or calcium lactate may serve to control pruritus, and sometimes to mitigate urticaria. *Digitalis* and *strophanthus*, the latter especially, are useful in regulating cardiac action, the indications being familiar. When other measures have not proved sufficient to quiet the heart—especially when the patient is first put to bed, and, later, when modified activity is first resumed—small doses of *strophanthus* may be used continuously. Better than any drug, however, during rest, and also in the rest periods that punctuate activity, is the application of a *precordial coil* through which ice-water is allowed to run. The *ice-bag* is a convenient, but less effective and somewhat clumsy, substitute. In some instances the ice-bag or coil may be more effectively applied to the cervical or cervicodorsal (thoracic) spine; or the precordial and spinal applications may be coincident or alternating.

Another drug useful in many cases, sometimes alone and sometimes in association with *digitalis* or *strophanthus*, is *cactus*. This is talking heresy; but I have records, including blood pressure measurements and tracings, showing the effect of a good cactus preparation in reducing abnormal pulse frequency, correcting arrhythmia and elevating blood pressure, especially in cases of Graves' syndrome and allied conditions. It is not often that *aconite* or *veratrum viride* becomes indicated in Graves' disorder, when rest and hydrotherapeutic measures have been instituted. In exceptional cases the familiar indications for these drugs may be presented. I have no experience with the use of *atropine* in this disorder, but I have heard it commended. Theoretically, it should be "guarded" with a *digitalis* drug.

**TOPICAL TREATMENT.** Is it, or is it not, advisable to attempt to reduce the goitre by local measures? I believe that it is, in many cases; and despite the fact that the internal administration of iodides usually aggravates the Graves' phenomena, I have observed no bad results, but only good result or no result, from topical applications of *iodine* preparations. Of these, the solution of iodine in liquid saponified petrolatum seems to be the best. Interesting theoretic considerations are suggested by this fact; but I will only

say that if the gland has hypertrophied in response to a demand from the system for the storing of iodine therein, so that this element may be delivered into the blood stream in an acceptable form, the artificial supply may enable it to reduce its activity.

*Electricity* has been utilized in various ways. Cataphoric, or as it is now termed, ionic, application of iodine has been made; the galvanic current has been passed through the gland, and applied over the neck in the neighborhood of the cervical sympathetic. In my own hands, the most satisfactory form of electric application—in that minority of cases in which any such treatment has seemed necessary—has been the high frequency discharge from an Oudin “resonator” in connection with a Tesla coil, Leyden jar battery, and static influence machine. Sometimes the electrification is directed to the goitre; sometimes to the back of the neck in the neighborhood of the *vertebra prominens*; sometimes to both. This application, however, has been used only in mild, early cases, in which absolute rest has not been indicated; or else, when the improvement has so far progressed that rest may be intermitted or given up; for it means that the patient should be able to visit the physician’s office two or three times weekly. It is of auxiliary benefit, but would not alone bring about recovery. How lasting the result may be one is not yet in position to say, as I have used this particular modality only during the last three years.

There are many other medicinal and physiological measures of more or less benefit in certain cases of Graves’ disorder, but those discussed or mentioned are sufficient to indicate the general character of the non-surgical treatment that has been found of service. It is not specific, although it is special; and it is highly individualized.

SERUMS, ETC. Before concluding, a word should be said as to the various serums and antibodies that have been proposed and used. My own experience with *Rogers’ and Beebe’s serum* has thus far been inconclusive; although it is only fair to say that I speak after a very limited trial. It produced remarkable, but not permanent, good results in two cases; and failed entirely in two other cases. That it has great possibilities cannot be gainsaid; and one should resort to it unhesitatingly, in any case in which cytotoxicity seems to be necessary.

*Rodagen*, a preparation made from the milk of thyroidectomized goats, I have used in but a single instance; that of a woman who was steadily improving under rest and treatment with thymus gland and strophanthus, but who became impatient at the prolonged restraint. There was immediate recurrence of subjective feebleness, anorexia, insomnia, and rapid action of the heart. The thyroid gland, which had been reduced, enlarged again, and considerably, in the course of a few days. The rodagen was stopped and the patient again improved. A month later it was again

administered in smaller quantity, but with the same untoward result. The original treatment was resumed and the patient made complete recovery, which has now lasted for some seven years. This would appear to give color to the theory that in this case at least, the enlargement of the thyroid gland was a compensatory, defensive hypertrophy, the necessity for which vanished with the administration of the thymus preparation.

*Antithyroidin* and *thyroidectin* have also failed in my hands, although neither has been given extended trial. The necessity to do so has not been evident when good results were obtained without them, and surgery has seemed preferable in the cases that did not seem suited for, or did not yield to, the medicinal and hygienic management that has been outlined.

SUMMARY. To sum up, Graves' syndrome is a complex disorder, having many varieties, a multiple etiology, and an obscure pathology. The goitre is an incident, and the disorder may exist without it. When goitre occurs, existing symptoms are usually aggravated and new symptoms added.

Surgical treatment rarely becomes necessary in cases recognized early. In approximately 15 to 20 per cent. of cases, surgery is made necessary by failure or inability to institute prompt, or proper and persistent, non-surgical treatment. In about 5 per cent. of cases surgery may become necessary, despite early and skilful hygienic and medicinal management.

The first element in treatment may, therefore, be stated as *early diagnosis*. Cases of which the true nature is not recognized are likely to be termed "neurasthenia," "hysteria," "nervousness," "anomalous neurosis," "nervous dyspepsia," and the like. Adequate treatment may thus be not instituted until late; and sometimes, too late. This is probably owing, in part at least, to the unfortunate title "exophthalmic goitre;" for both goitre and exophthalmos are usually late signs.

There is no specific; but certain useful measures may be organized into a form of special procedure.

Non-surgical treatment is usually prolonged. Its keynote is *individualization*. It must be patient and persistent. Its principal element is *rest*; to be modified according to circumstances. Rest must be mental as well as physical, and must include correction of ocular errors (eye-strain) and removal of all sources of reflex irritation. Instituted under diagnostic error, it is equally beneficial. Fresh air and regulation of diet are necessary, much as in pulmonary tuberculosis. Active elimination must be maintained. Educational exercise of the vasomotor system by hot and cold applications is always of benefit. Under such management, with perhaps occasional symptomatic medication, somewhere from 25 to 30 per cent. of all patients may be expected to get well—the cases of so-called spontaneous recovery.



The application of ice-water coils over the heart and over the cervical spine, the administration of trustworthy preparations of well-chosen organ-extracts and various forms of auxiliary medication; with perhaps the use of certain mechanical manipulations, topical applications, and electric modalities, will increase the number of recoveries to 80 per cent. or more.

---

## INFECTIONS FOLLOWING TONSILLOTOMY WITH A CONSIDERATION OF THE FORMS OF SUCH INFECTIONS.

BY HENRY KOPLIK, M.D.,

NEW YORK.

DURING the last twenty-five years our knowledge of infections with the tonsil as a port of entry has been enlightened to a considerable extent, both from an experimental and clinical point of view. The evidence that such infection takes place is overwhelming. Speaking of nurslings and children Gundobin<sup>1</sup> asserts that the tonsils have a pathological significance due to, on the one hand, their hyperplasia, and, on the other hand, their capability of transmitting certain infections. We meet hyperplasia of the tonsillar tissue not alone most frequently from the fourth to the eighth year of life, but in the newborn and the adult. The tonsils, the pharynx, and nasopharynx with its adenoid tissue, the peritonsillar tissue, and the lymph nodes and lymphatic tissue of the retropharynx form one connecting ring by which infections may pass from the tonsil into the general circulation. I will not discuss the question as to whether the tonsil must be traumatized in order that infections may penetrate into the deeper structures. This seems to me a question of rather academic interest in the face of the clinical facts that infections traceable to the tonsils may be closely connected with the appearance in quick sequence of rheumatism, endocarditis, pneumonia, nephritis, orchitis, appendicitis, etc. The literature, which is quite extensive, is not lacking in furnishing evidences of infections as hinted above. Moreover, forms of so-called cryptogenetic infections are traced to old tonsillar foci. Gwosdinsky<sup>2</sup> reports such a case, the principal symptoms of which were numerous large hemorrhages into the skin, with staphylococci circulating in the blood and suppurations of various organs traceable to an old retropharyngeal abscess. Tischutkin<sup>3</sup> publishes a fatal case of bacterial sepsis as a result of

<sup>1</sup> Trentise.

<sup>3</sup> Wratseh, 1897.

<sup>2</sup> Rus. Arch. of Path., 1897, Band iii.

tonsillar infections, and emphasizes the importance of the tonsils as a source of cryptogenetic infection. Baup<sup>4</sup> injected the tonsils with tubercle bacilli, and showed that these could pass to the lymph passages of the neck and mediastinal lymph nodes. Grober<sup>5</sup> did much the same work with carmine. Menzner<sup>6</sup> investigated the peritonsillar tissue in cases of rheumatism, and concluded that by this route bacteria obtained access to the blood current, causing endocarditis and rheumatic manifestations; under certain conditions the normal protective arrangement of the lymphatic pharyngeal ring is overcome and bacteria pass in a virulent state into the circulation. It is not yet clear why these things occur in certain individuals and not in others. It seems to me that much more is needed than a simple infection of the tonsils to presuppose a systemic infection. We have all seen patients repeatedly attacked with tonsillar infection, and yet no systemic invasion resulting in choreal, endocarditic, or rheumatic manifestations occurred. We must, rather, assume some systemic individual idiosyncrasy which allows of such a result, else the simple fact of the presence of a tonsillitis would be universally disastrous.

Years ago Packard<sup>7</sup> showed, from a purely clinical standpoint, the sequence of endocarditis and tonsillar infection; and, later, Forcheimer<sup>8</sup> cited instances of systemic infections including appendicitis and infectious jaundice as a sequence of tonsillitis. The appearance of an endocarditis in the course of a tonsillar infection is certainly, today, not a novel experience—on the other hand, general severe septicemia following catarrhal angina is a matter of record (Tollens).<sup>9</sup> Such cases are exceptional, but they do occur. An angina may result in simple swelling and redness of the fauces (bacteremia); or in severe inflammation of the lymph nodes with secondary suppurations, as appendicitis, osteomyelitis, endocarditis, and signs of sepsis of the internal organs without bacteremia; or there may be angina with endocarditis, acute nephritis, cholecystitis, encephalitis, arthritis, where changes grossly clinical in the neck are slight (Kretz),<sup>10</sup> and there is no bacteremia.

Lingelsheim<sup>11</sup> found streptococci constant in and on the tonsils in the normal pharynx and nose, and this fact is frequently confirmed in the literature. The least irritation increases in numbers these normal habitants of the tissues. It is only additional evidence to quote the literature to any greater extent to prove our thesis—that the tonsils play a role in systemic infections which daily experimental, pathological, and clinical data go to confirm. The

<sup>4</sup> Les Amygdales porte d'entrée de la tuberculose, Thèse, Paris, 1900.

<sup>5</sup> Deutsch. Arch. f. klin. Med., 1900.

<sup>7</sup> AMER. JOUR. MED. SCI., 1900.

<sup>9</sup> Zeit. f. Ohrenheilk., 1902.

<sup>11</sup> Loc. cit.

<sup>6</sup> Deutsch. Auld Woch., 1901.

<sup>8</sup> Amer. Ped. Soc. Trans, 1902.

<sup>10</sup> Zentralbl. f. Path., 1906, Band xvii.

whole mass of literature may be summed up to show that tonsillar infections may first cause simple febrile disturbances without septicemia, they may result in systemic infections causing endocarditic, rheumatic joint, and choreal manifestations, and finally, as in the case of Gwosdinsky,<sup>12</sup> septicemia with hemorrhagic manifestations and fatal issue.

If the tonsil *in situ* is such a source of danger as a port of entry of infections, the organ, when the subject of traumatism or operation, opens up a whole area which easily takes up infection. In recent years it has been my observation that after tonsillectomy or enucleation of the tonsils, with or without the removal of the adenoid growths in the nasopharyngeal space, certain forms of infection are apt to arise. It is surprising that those whose work lies in this special field of surgery are not impressed with this danger. The nose and throat surgeons, as a rule, do not see all of their cases after operation, and inquiry among them elicits very little data as to the infections which are the theme of this paper. In fact, in one case a surgeon asserted that he had performed a thousand or more operations on the tonsils and adenoids without once having observed a case of infectious fever following the operation. Inasmuch as the statement was made in a conference, and the case on which he had operated was running a septic temperature subsequent to the operation, it may be seen that these cases have not as yet received the full attention they call for.

There are three forms of infection which I have seen following the removal of the tonsils, or adenoids, or both:

1. After an operation the patient may appear to be doing well, but on the second or third day begin to run a temperature of varying severity. A careful examination of the chest and throat fails to reveal any cause for this temperature, and in the cases which I have in mind the heart remains normal and there is no development of a murmur nor any signs of endocarditis. The lymph nodes in the neck may not be enlarged, the patient recovers after a week or more, and no signs of any other lesion are found to account for the run of temperature. In the cases I refer to the ears are blameless, and here I will exclude from any consideration those numerous cases in which, after operation, the ears become the seat of inflammation by apparent extension of inflammatory processes of repair, or inflammatory exacerbation from the pharynx. Not long ago I was called to see a case of a boy, aged about nine years. He was quite well before his tonsillectomy; the physician had advised ablation of the tonsils as a hygienic measure. The operation was neatly and successfully accomplished. After twenty-four hours the patient began to run a high temperature, 103° to 104°. On examination the physical condition of the patient showed

absolutely nothing. When I saw the patient the necrotic areas generally seen after operation had fully cleared off and the throat looked clean. The patient ran an obscure temperature for two weeks and then recovered without ill effects on the heart and no rheumatic manifestations. Since seeing this case I have heard of and seen similar cases, but inasmuch as I have not been allowed to examine the cases myself I cannot vouch as to the absence of other lesions, as in the typical case related. I have the conviction that such cases are not uncommon.

2. A second set of cases are those in which, after ablation or enucleation of the tonsil, the patients run a moderately high temperature for weeks and develop cardiac murmurs, or even in a short time after operation develop the signs and symptoms of a malignant form of septic endocarditis, and die. Of this latter form of infection it can be said that they must be extremely rare, but they certainly do occur.

The following is a very instructive example of such an infection, which I published some years ago:<sup>13</sup> A boy, aged ten years, suffering from manifestations of rheumatism in the form of a mitral regurgitant murmur of old standing, had a mild form of chorea. While the chorea was in progress, the patient, being up and about, was operated upon and the tonsils and adenoids were removed. Three days after the operation the patient was seized with a chill and fever and an exacerbation of the chorea. Examination of the heart at this time showed a peri-endocarditis. In the second week he became delirious, complained of precordial pain, and ran a high temperature. He developed, also, petechiæ, and died after an illness of two weeks. This case was seen by others in consultation, and the opinion was unanimous that the operation had precipitated the violent form of sepsis from which the patient succumbed.

A much milder form of sepsis, but just as disquieting, occurred in a case of a child, aged seven years. She was in perfect health. Her tonsils were not large, but the surgeon said they were the seat of erosions, and advised removal in spite of the perfect condition of the child. The tonsillar tissue, which was successfully removed by enucleation, was not great in bulk. The child apparently weathered the operation successfully. Three days after the operation it was noticed that the child was not herself, and investigation revealed a temperature running quite high. After some days of illness I saw the case. She had been running an irregularly remitting temperature. Her fever would mount as high as 104° to 105°, and fall to almost the normal. Under antipyretics the temperature would stay at or nearly the normal for one or two days, and then mount again. The throat at the time I saw the patient had cleared of all necrotic tissue. The patient had a

<sup>13</sup> *Diseases of Infancy and Childhood*, 1902.

flushed appearance, and after a week of fever had lost ground physically—otherwise she was in good spirits. There was a slight bruit over the apex and base systolic in time, and on one conjunctiva there was a doubtful petechial spot. A blood culture failed to reveal bacteria, but the course was that of a mild endocardial infection, lasting over three weeks, with recovery. This case was seen, also, by others and the opinion of a postoperative infection appeared to be conclusive. All other forms or causes of infection, such as typhoid, or even mild chest infections, or paratyphoid infections, were excluded and not entertained. The sequence of the febrile attack so immediate upon operation, the absolute exclusion of everything pointing to other organs, left only the one conclusion of a postoperation infection.

3. The third form of septic infection following tonsillotomy or adenectomy, which I have seen resembles more a hematogenous borne infection, and is of interest in view of the case cited in the first part of this paper by Gwosdinsky, in which the sepsis took the form of extensive hemorrhages throughout the body.

*Case history:* Female, aged five years, admitted to the service January 17, 1912. Discharged February 27, 1912.

*Family history:* Negative; no hemophilia.

*Past history:* Measles when aged two years; varicella when aged four years; never bled profusely; always a mouth breather. Three weeks before admission her tonsils and adenoids were removed at an institution devoted to the treatment of diseases of the nose and throat.

*Present history:* Since the day following the operation the child had been running a temperature of 104° to 105°. Two weeks before admission she began to cough, with mucoid expectoration, but on examination no distinct pneumonia could be established. Three days before admission to the hospital patient began to bleed from the lips. Ecchymosis appeared on the skin of the back, and two days before admission the patient bled profusely from the rectum. This intestinal hemorrhage was repeated several times, and for this she was transferred to the hospital. There were no chills, no sweats.

*Examination on admission:* The patient was fairly well nourished, but anemic. There were several large ecchymotic areas on the back, buttocks, and thighs, and petechiæ over the upper and lower extremities. The rectum was filled with blood clots. There was bleeding from fissures in the lips. The conjunctivæ showed petechiæ. The cavities where the tonsils were located were raw surfaced and blue, there was blood in both nostrils. The post-cervical and submaxillary glands were palpable. The lungs showed a dull area over the lower lobe on the left side, behind, with a few crepitant rales, otherwise negative. The heart showed a slight systolic blow at apex.

On admission the blood showed red blood cells, 3,744,000; leukocytes, 22,000; polymorphonuclear leukocytes, 72 per cent.; lymphocytes, 25 per cent.; eosinophiles, 3 per cent.

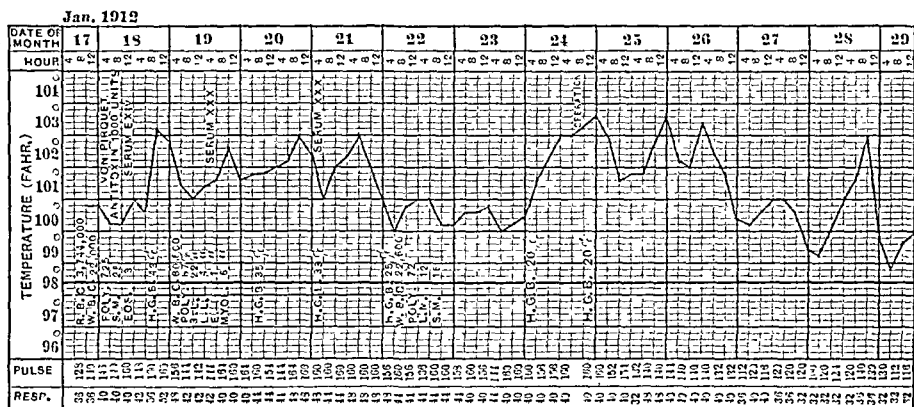
Subsequent to admission the patient ran a febrile course and more petechiæ developed over the surface; one or two hemorrhages occurred from the bowel. The heart murmur became more pronounced, and was heard over the whole precordium and at the apex. The pallor increased, the hemoglobin steadily diminishing to 25 per cent.

On January 24, the anemia was increasing in spite of the fact that no new petechiæ appeared, and no additional hemorrhages from the bowel occurred after the injection of 75 c.c. of human blood serum the first three days after admission. By January 24, the hemoglobin sank to 20 per cent. A direct blood transfusion was performed, the father being donor, by Dr. A. Moscovitz, of Dr. A. Gerster's service. Hemoglobin rose to 65 per cent., wound healed by primary union.

The subsequent history was one of uninterrupted convalescence, the lung signs persisting for some time.

On discharge of the patient the blood examination showed: Red blood cells, 5,560,000; leukocytes, 12,800; hemoglobin, 88 per cent. Differential count: Polymorphonuclears, 38 per cent.; lymphocytes, 61 per cent.; eosinophiles, 1 per cent.

A blood culture taken before the transfusion and during the run of temperature failed to show the presence of bacteria.



Temperature curve of a case of hemorrhagic sepsis after tonsillectomy and removal of adenoids in a child, aged five years. Recovery after transfusion.

From a study of this case it will be seen that the patient ran a temperature which followed immediately upon the operation of tonsillectomy and adenectomy. She was seen in the week or two subsequently and no lung or other condition could be made out. When I saw the patient at her home with the attending physician she had begun to develop the new symptoms of

hemorrhage from the bowel, which was profuse and exsanguinated the patient. In addition there were petechiæ all over the surface of the body and on the conjunctivæ, a systolic murmur was heard at the apex and over the precordium, and there was a high fever. In the hospital the hemorrhages under administration of serum (normal human) ceased, but the temperature, as seen from the chart, continued. The hemoglobin, in the absence of further hemorrhage, diminished to 20 per cent. The patient also developed more marked signs after admission of a bronchopneumonic process over the lower lobe of the left lung behind. She was still running a temperature of 103° and sinking, when I determined to have a direct transfusion performed. This was done, the father being donor. After the transfusion the temperature gradually sank to the normal and from this time the patient remained convalescent, and was discharged in a normal condition both as to her blood and physical state. The murmur which was present on admission completely disappeared after transfusion, proving conclusively its hemic origin. The culture of the blood taken in the course of the illness was negative for bacteria, and, on account of the extremely critical condition of the patient, was not repeated.

Here is a case of true hematogenous sepsis following tonsillotomy and adenectomy in an institution, performed under the most excellent hygienic conditions. There was in this case no history of hemophilia or any bleeding tendencies in the family or the child. The case resembles very much those cases which we meet from time to time in which leukemic blood conditions seem to have followed some operation on the tonsils, instances of which are cited in the literature. The case is unique, inasmuch as the transfusion was performed for a progressive anemia which continued after the hemorrhages on the skin and from the intestine had ceased, and which recovered in the face of an evident sepsis in progress at the time of transfusion. The transfusion was performed as a last resort, to save the life of the patient.

In this paper I have called attention to three distinct forms of sepsis which followed upon surgical removal of the tonsils:

1. The form which runs an obscure fever for a week or more without causing any endocarditic or other lesions.

2. Those cases which run a temperature and combine with them the manifestations either of a mild infectious endocarditis, or in which, as in the case of chorea, the endocarditis takes on a severe infectious (or, as it is called, malignant) type, with subsequent fatal issue.

3. A third form of sepsis is that in which the infection is evidently severely hematogenous and causes destructive blood changes, with signs of sepsis such as profuse hemorrhagic ecchymotic areas on the surface of the skin, petechiæ, severe hemorrhages from the bowel, and areas of bronchopneumonia.

THE ANATOMY AND RELATIONS OF THE TONSIL IN THE  
HARDENED BODY, WITH SPECIAL REFERENCE TO THE  
PROPER CONCEPTION OF THE PLICA TRIANGULARIS.  
THE PRINCIPLES AND PRACTICE OF TONSIL  
ENUCLEATION AS BASED THEREON.<sup>1</sup>

BY GEORGE FETTEROLF, M.D., Sc.D.,

ASSISTANT PROFESSOR OF ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; LARYNGOLOGIST TO  
THE PHIPPS INSTITUTE OF THE UNIVERSITY OF PENNSYLVANIA AND TO THE WHITE HAVEN  
SANATORIUM; CONSULTING LARYNGOLOGIST TO THE PHOENIXVILLE HOSPITAL, THE  
KENSINGTON HOSPITAL FOR TUBERCULOSIS AND THE EASTERN PENNSYLVANIA  
STATE INSTITUTION FOR THE FEEBLE-MINDED AND EPILEPTIC; FELLOW OF  
THE COLLEGE OF PHYSICIANS OF PHILADELPHIA.

(From the Henry Phipps Institute and the Laboratory of Anatomy of the University of  
Pennsylvania.)

It is a poor and unproductive three months in laryngological literature which does not furnish something new in regard to tonsil removal, either in method or in armamentarium, and most of us have a collection of instrumental junk which we have acquired from time to time in the endeavor to improve our technique. This certainly shows that the operation is neither simple nor easy and gives rise to the question—has it been the lack of proper instruments so much as other factors, which has made so many operations in the past more or less inadequate procedures? Have not all of us been dissatisfied at times with the operative results of some of our cases? Have not all of us had patients who have had tonsillitis and quinsy after we had operated on them? Under these circumstances might it not be well to consider what should be our aim, what are the reasons for failure, what are really the conditions to be met and how may the obstacles be overcome? It does seem as if we should aim at but one result, namely, complete removal of the tonsil, including the capsule. Many, perhaps, will disagree with this, but if complete removal were as easy as is partial, and if it could be shown to be no more or even less dangerous, how many then would fail to agree? In doing an appendectomy, the surgeon does not leave half the diseased or even a healthy half of the appendix in place; in operating on diseased cervical lymph nodes, we would not consider for a moment cutting away three-quarters of the diseased tissue and leaving the capsule. The same surgical principles which apply to diseased tissue elsewhere in the body should apply to the tonsils, and it seems to the writer that the weight of argument is in favor of complete tonsillectomy as the rule, and partial tonsillectomy as the exception.

<sup>1</sup> Read before the Section on Laryngology and Otology of the College of Physicians of Philadelphia, March 20, 1912.



Since a true appreciation of the undesirability of the presence of a diseased tonsil has become more and more generally known, whether on account of its being a portal of entry for pathogenic organisms, whether for intrinsic disease, whether for repeated acute disease, or for mechanical obstruction, the importance of good surgical treatment has become more generally recognized. The necessity for complete extirpation is becoming more and more realized as being desirable, except possibly in the old, in those with heart lesions, in those unable to take a general anesthetic, or in those cases of chronic lacunar disease in which removal of portions of the tonsil will open the tonsil fossæ and the diseased lacunæ.

**TONSIL ENUCLEATION NOT A ONE-INSTRUMENT PROCEDURE.** In spite of our recognition of this principle, how often is it that our operations are incomplete. I fancy that at times we are tempted to feel that if we use the latest and most approved appliances we are doing all that can be expected. There has been and still is a tendency to regard the operation as a "one-instrument" procedure, but it is no more so than is circumcision. For example, the punch for a while and then the snare had the ascendancy, yet recently I have seen 4 cases which had been operated on by able exponents of the snare method, 2 of which were from Philadelphia and 2 from neighboring large cities. In each one of these really large masses of tonsil had been allowed to remain. The error in these cases was in the assumption that one instrument could do it all, that it was necessary only to get the snare beyond the equator and it would follow the surface of and shell out the tonsil. The snare has its place in tonsil enucleation, but in the writer's opinion, not as a dissector, not as an instrument to do work that can be done better by other appliances.

Several attempts have been made to do the operation with a single maneuver, necessitating some such instrument as the tonsil-lotomes of McKenzie, Mathieu, Ballenger, or Sluder, or the "tonsillectome" of Beck. If such a device could remove all of the tonsil all of the time it would be ideal, but a study of the anatomical relations of the tonsil *in situ*, of the extirpated tonsils themselves, and of the throat results of such "royal road" operations (and this term is used with no disrespect to the sincere and earnest workers who have devised such appliances), such study leads one to the conclusion that no such instrument either has appeared as yet or possibly can be devised. This criticism the writer can make personally only in connection with the McKenzie and Mathieu instruments, since he has not had the opportunity of seeing any cases operated on by means of the Sluder or Beck instruments. However, Beck<sup>2</sup> himself states, "I wish to say that occasionally

one finds tonsils that cannot be removed by the instrument I am describing, or by the Sluder or the Ballenger instrument, and require being dissected in the usual way." Another opinion along the same line is that of St. Clair Thomson<sup>3</sup> who says, "Dissection is necessary for tonsils which cannot be guillotined."

Estimates as to the number of tonsils which can be removed completely with the guillotine alone vary from 45 per cent. by Whillis and Pybus, who favor the method, to 2 per cent. by Hett, who advocates enucleation by dissection.<sup>4</sup>

Hett<sup>5</sup> has made a careful study of this question and his findings are interesting:

"Now if we examine a series of tonsils, removed by the guillotine without previous separation of the pillars, we shall find that the capsule has been cut through, and consequently some tonsil has been left in a large proportion, and this whatever the means employed, whether by volsellum traction and guillotine, or by forcing the tonsil through the guillotine ring from without." "I have collected a large series removed by experts on the staffs of our leading special hospitals, and the result has been that very few tonsils thus removed have the capsule complete."

REASONS FOR FAILURES. A detailed study of the tonsil in the living patient and in the dead subject soon convinces one that it is too variable in size and situation and its extraction is too complex a matter to be accomplished invariably by means of a single device. Such an appliance in the hands of its skilled inventor may be remarkably effective, but the advocacy of the general adoption of any such instrument is harmful in that it results in its use by unskilled tyros in all of their cases, with the result that many incomplete operations are performed and more tonsils are added to that long and shameful list of those which have "grown again."

There are other factors that have caused so much bad work to have been done, and in looking back the writer can see clearly the reasons for it in his own case. They were mainly surgical timidity, fear of hemorrhage, ignorance of important anatomical points, a lack of careful study of the results of the operation at the time of the operation, a failure to study the case after the operation, the occasional brilliant clinical result of an incomplete operation, and translation of the occurrence of an occasional accidentally complete extirpation into a hope that the methods used would be successful the next time and the next and the next.

The phrase "surgical timidity" is used advisedly. We nose and throat men are unfortunate in our surgical work, in that in

<sup>3</sup> Jour. of Lar., Rhin., and Otol., October, 1910, 541.

<sup>4</sup> J. S. Fraser, The Faucial Tonsils, with Special Reference to their Removal by Enucleation Trans. Medico-Chirurgical Society of Edinburgh, 1910-1911, 151.

<sup>5</sup> Jour. of Lar., Rhin., and Otol., November,

1910, 561.

so many instances we have to leave behind us open surfaces from which highly vascular structures have been removed. The wish, no doubt, often comes to us that we were working in soft tissues where we could see clearly, secure and tie any vessel that is severed in the course of the operation. Again, the blood we are causing to flow is interfering with the vital function of respiration and we naturally desire to get this over with as soon as possible. Then, if hemorrhage does occur it is at a point that is always awkward, sometimes difficult to determine and reach, and we are inclined to hasten our work so as to be able to assure ourselves as soon as possible that bleeding has ceased. All these combine to disturb the calmness with which an operation always should be approached and the consequence too often has been hurry and a bad result. There is present, too, the perhaps unformed wish for a quick return of the throat reflexes so that the blood and secretions in the throat shall be expectorated. For this reason the anesthesia may be skimped, and not prolonged so that the postoperative condition can be thoroughly examined, all defects corrected, and all bleeding points closed before the patient leaves the table.

Fundamentally, the great desiderata in the tonsil operation are completeness and reasonable celerity, combined with safety both during and after the operation. The inadequacy and uncertainty of the guillotine are daily becoming better realized and many operators are in the throes of transition from the use of this instrument to enucleation by dissection. The result is that there are advocated and performed today many methods of tonsil removal, so many as at first to make one wonder why. The inclination is to reach one of two conclusions, either that all methods are effective, or that none are. Probably a middle ground in this respect is the correct one, namely, that all methods result in the removal of some of the tonsil, and that either no method invariably results in the removal of all of the tonsil or is regarded as being sufficiently easy, safe, or clearly defined to be universally adopted with comfort.

SCOPE OF PRESENT PAPER. Much light has been shed on human and especially on visceral anatomy and its clinical application by the adoption of the method of hardening viscera *in situ* before they are dissected. Studies of various problems in the chest have proved to be of such great interest that the writer instituted a series of similar observations on the tonsil, with the idea of satisfying himself as to just exactly what surgical problems were present. After doing this the next attempt was to correlate these findings with the operative resources at hand and to deduce therefrom an always efficient method of attaining the desired end. In other words, the endeavor has been first to discover the principles which must guide, and then to elaborate the practice which should be followed.

The operation has not been studied hitherto from this point of view. It has been a step-by-step development, as each successive procedure has improved on the preceding one. The various methods of operating advocated today represent practice only, not principles. Their evolution has been purely clinical, and no really minute application of the present-day methods of anatomical research has been made to the tonsil and its surgery. The discussion<sup>6</sup> following Hett's paper at the 1910 meeting of the Laryngological Section of the British Medical Association is most revealing in this connection.

The first part of the present communication is mainly anatomical in character and represents the study of the faucial region in bodies which before dissection were injected with 30 per cent. formaldehyde solution. It is a fair assumption that conditions found in the throat in such cadavers are similar to those present during life, and as the result of this study it has been found possible to add a number of details to the current anatomical descriptions.

The second part consists of a description of the operation of tonsil enucleation as the writer performs it, each step of the operation being given in detail along with the reasons for its adoption. It represents the deductions of considerable anatomical study and of much unsatisfying operative work, and is presented because the writer feels that each step and precaution have a rational anatomical basis. In addition, the procedure as a whole has proved to be an efficient method of complete enucleation of the tonsil in every case. As regards safety, there are several anatomical reasons why it should be safer than the majority of advocated methods; these will be discussed in detail further on. No new instrument is recommended; much of the suggested technique is not original or new, any instrument or procedure which was found to be of use having been adopted or adapted. The writer would like to emphasize particularly the suggested interpretation of the *plica triangularis*. It has not been advanced before and it is mentioned at this point principally on account of its importance in always making a correct start when performing the operation.

#### ANATOMICAL CONSIDERATIONS.

In the endeavor to determine exactly what are the conditions in the faucial region during life and with the mouth closed a number of dissections were made of hardened heads in the Laboratory of Anatomy of the University of Pennsylvania. From these preparations the following facts were elicited, some of them of purely academic and others of practical interest.

<sup>6</sup> Jour. Lar., Rhin., and Otol., October, 1910, 540.

**THE FAUCIAL REGION.** After splitting a head into halves by a median sagittal section it was found impossible to see any part of the faucial region because the tongue completely filled the buccal cavity. To reveal the lateral wall the half tongue in the section had to be removed (Fig. 1). When this was done considerable search was required in numerous instances to find the classic landmarks, namely, the pillars of the fauces and the tonsil. The curve of the hard and soft palates was found to be continued regularly and practically uninterruptedly, not only backward to the posterior pharyngeal wall, but also laterally downward to the base of the tongue. Careful exploration was necessary to determine definitely the position of the anterior pillar, the plica triangularis, the tonsil, and the posterior pillar.

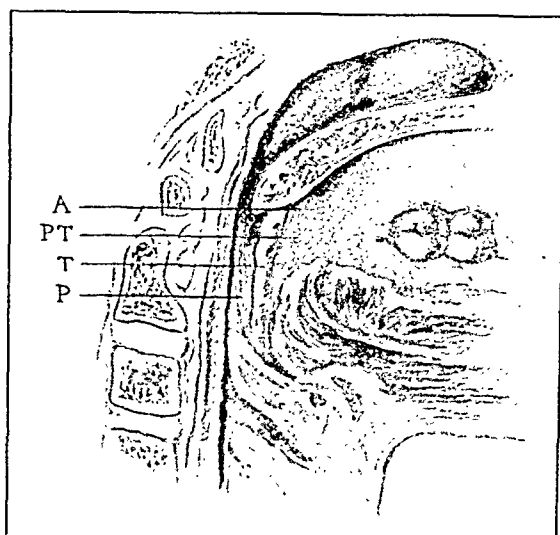


FIG. 1.—Left faucial region: *A*, site of anterior pillar; *PT*, plica triangularis; *T*, tonsil; *P*, palato-pharyngeus.

**THE ANTERIOR FAUCIAL PILLAR.** Instead of standing out sharply into the mouth, as is commonly depicted, this structure is lost in the lateral wall (Fig. 1). Its identification was possible only at its lower part and even then as but a very slight semi-cylindrical elevation. Occasionally an indefinite dark streak indicated the presence and position of the muscle underlying the mucosa, this streak probably corresponding to the normally reddened area of the pillar. The evident conclusion is that when the mouth is closed the anterior pillar is buried for the most part in the lateral wall. Only when the mouth is opened and the tongue depressed does it project inward as a more or less sharp edge. The assumption of the latter position is probably due to two factors: (1) The anterior pillar is limited in length and, consisting as it does of the palatoglossus muscle covered by mucosa, is attached

above to the soft palate and below to the tongue. In passing from its upper to its lower anchorage it curves widely outward into and is lost in the lateral wall. When the distance between its ends is lengthened the natural result is to straighten out the curve,

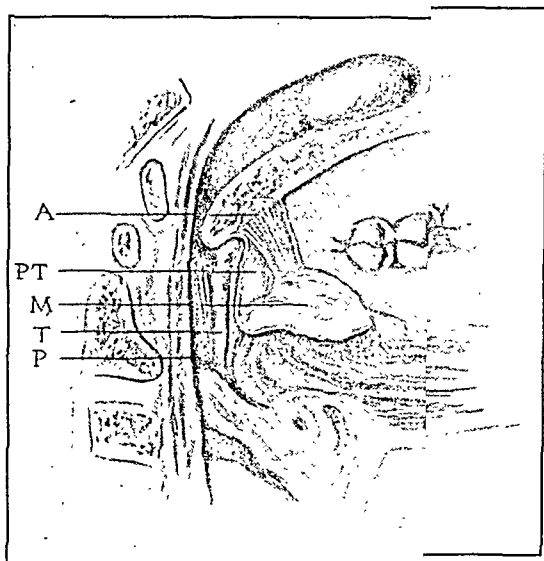


FIG. 2.—Left faucial region, with mucous membrane reflected from palato-glossus and plica triangularis; *M*, reflected mucous membrane; *A*, palato-glossus; *PT*, plica triangularis; *T*, tonsil; *P*, palato-pharyngeus.

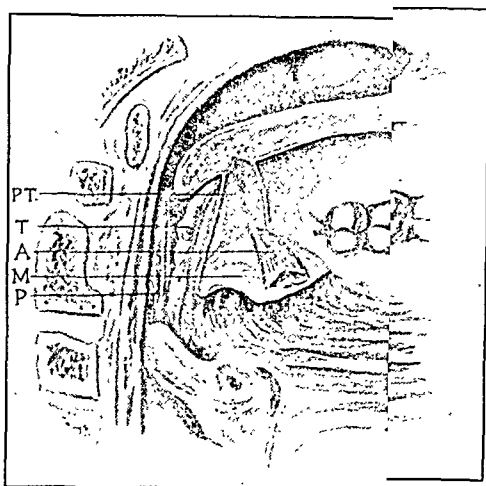


FIG. 3.—Left faucial region, with mucous membrane and palato-glossus reflected; *M*, reflected mucous membrane; *A*, palato-glossus; *PT*, plica triangularis; *T*, tonsil; *P*, palato-pharyngeus.

to cause it to describe the arc of a much larger circle. The upper end being fairly fixed cannot move and the lower end moves with the tongue. When the mouth is opened and the tongue depressed the middle and lower portions have to move, and this they do toward the median line. (2) In lengthening the anterior pillar

the faucial recess is narrowed and the tonsil, particularly its lower part, pressed inward and, being adherent to the pillar, the tonsil carries the pillar inward with it.

**THE PALATO-GLOSSUS MUSCLE.** In the hardened head this muscle is found to be of the form of a three-sided prism, or, on cross-section, of a low isosceles triangle (Fig. 2). The base faces into the mouth, the anterolateral side abuts against the tissue of the soft palate, and the posterolateral side is in contact with and covers the anterior part of the capsule of the tonsil. The apex lies in the sulcus formed at the anterior margin of the tonsil (Fig. 3).

#### THE PLICA TRIANGULARIS.

The plica triangularis was so named by Wilhelm His, although it had been described previously by both Kölliker and Sappey; Kölliker speaks of it as a "valve-like structure."

His' description of it is "In the fetus of four or five months there arises from the free margin of the anterior faucial pillar a triangular fold whose apex blends with the palate while the base is inserted broadly into the lateral aspect of the tongue." "In the adult one can generally still recognize the region of the early plica triangularis as a smooth surface covering the anterior part of the tonsil. In other cases the original arrangement remains in a slightly changed form as a persisting plica triangularis and a no less marked recess situated above the tonsil."

The plica in the cadaver is sometimes difficult to find but usually it is readily identified, especially at its posterior edge, where the difference between its smooth mucosa and the lacuna-studded surface of the tonsil is marked (Fig. 1). Many authorities state that frequently it is absent, but in the writer's experience this is not the case, not a single instance ever having been noted in which it was not present. It varies greatly in size, but persistent search always has resulted in its being found. Of its three sides (Figs. 1, 5, 11) the anterior is attached apparently to the anterior pillar, the posterior runs downward and backward over the tonsil and the inferior either is inserted into the side of the tongue, or, in the case of a small tonsil and a large fossa, fades away in the lower part of the tonsillar recess.

All the authorities consulted agree in describing it as a fold of mucous membrane; quotations to this effect are unnecessary as reference to any text-book of anatomy will confirm the statement. Study by the writer of the tonsil in the office chair, at the operating table, in the cadaver, and under the microscope has convinced him that the accepted description is an error—an error of omission.

Both anatomically and clinically the plica is far more than a fold of mucous membrane. The true definition is this: *The plica triangularis is fundamentally that portion of the tonsil capsule which extends inward and backward beyond the anterior pillar of the fauces* (Figs. 4 and 5). Its free surface or surfaces are covered with a layer of mucous membrane, but there is never present any more mucosa than is sufficient to cover the basic fibrous tissue, this showing that the mucosa is a secondary element. If it is not

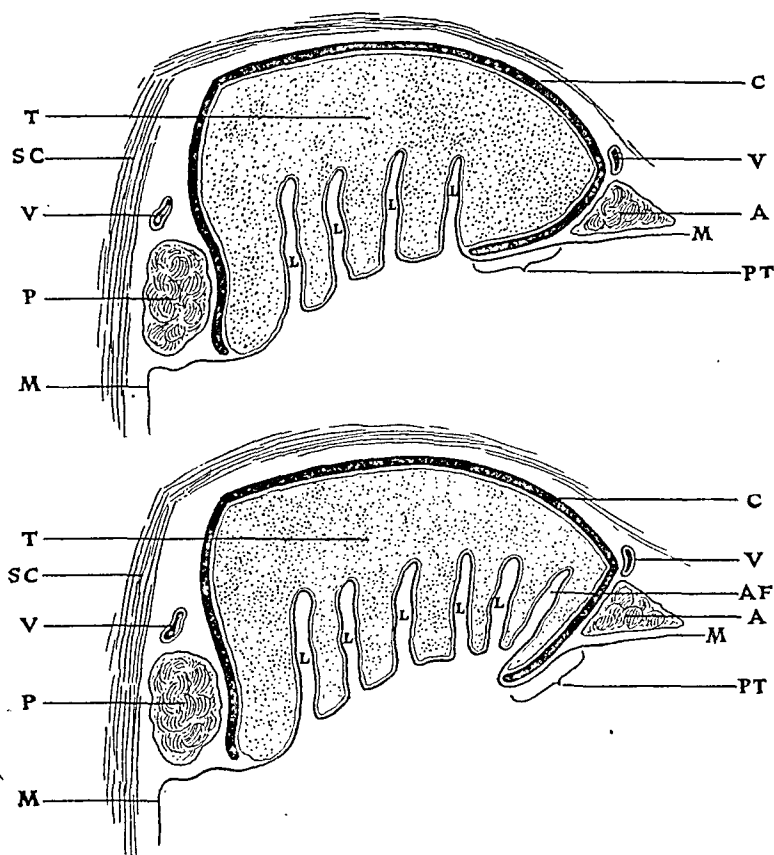


FIG. 4.—Diagrams of horizontal sections of left tonsillar region, viewed from above, the upper one showing the attached form of plica and the lower one the free form: T, tonsil; C, capsule; PT, plica triangularis; M, M, mucous membrane; L, L, lacunæ; AF, anterior tonsillar fossa; SC, superior constrictor; A, palato-glossus; P, palato-pharyngeus; V, V, main veins of tonsillar plexus.

attached throughout to the tonsil, that aspect of it which presents toward the latter is likely to have a more or less thick layer of lymphoid tissue between the fibrous and deep mucous layers, resembling in this respect any other portions of the capsule. It may consist, therefore, either of two, three or four layers—two, if it is attached throughout to the tonsil, and either three or four if it is free. In the case of two layers they are, from the surface inward, mucous membrane and fibrous tissue, in the case of three,



mucous membrane, fibrous tissue, and mucous membrane, and in the case of four, mucous membrane, fibrous tissue, lymphoid tissue and mucous membrane.

In those cases in which the mucosa passes directly from the inner edge of the plica to the tonsil, the latter frequently is called adherent. This designation is somewhat misleading as it creates the impression of old inflammatory disease, as in the case of adherent pleura or adherent appendix. Possibly a better terminology would be "free plica" and "attached plica." The apparent conditions present differ in a marked degree in the two forms, although the real difference is a slight one, namely, the presence or absence of a fossa or large crypt, as will be shown later.

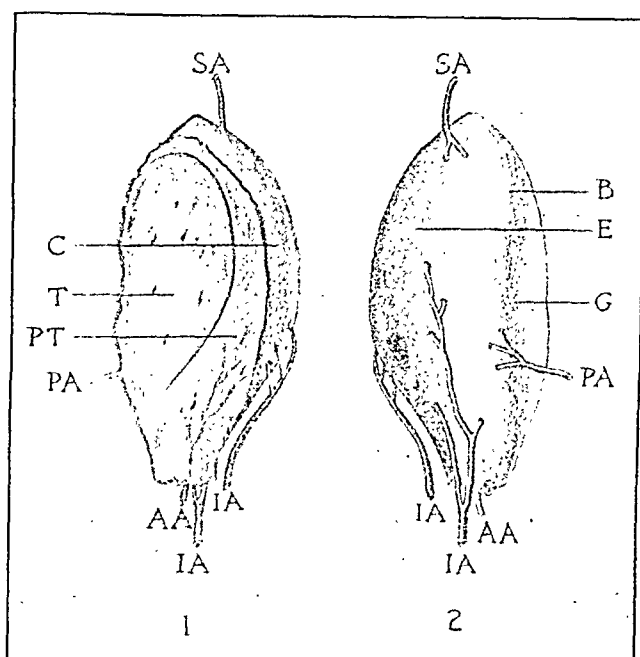


FIG. 5.—Actual shape of (left) tonsil, with arterial supply: 1, mesial aspect; 2, postero-lateral aspect; *E*, lateral surface; *B*, posterior surface; *G*, groove for palato-pharyngeus; *T*, tonsil tissue; *PT*, plica triangularis; *C*, capsule; *AA*, anterior tonsillar artery; *PA*, posterior tonsillar artery; *SA*, superior tonsillar artery; *IA*, inferior tonsillar arteries.

**THE ATTACHED PLICA.** When one of this type is traced laterally by dissection its layers are found to diverge at the inner margin of the anterior faucial pillar (Fig. 4). The superficial or mucous layer passes anterior to and blends with that of the pillar, while the deep or fibrous (capsule) layer dips beneath the posterior surface of the pillar and is found to be continuous with the rest of the tonsillar capsule (Figs. 6 and 7). Realization of these relations greatly simplifies the conception of the plica and not only emphasizes but clarifies its surgical value. If its mucous covering is removed at operation and the surface of its exposed fibrous

tissue is then followed laterally and beneath the anterior pillar, the operator is certain to be external to the capsule and in the proper operative tissue plane, namely, that between the capsule and the pharyngeal wall.

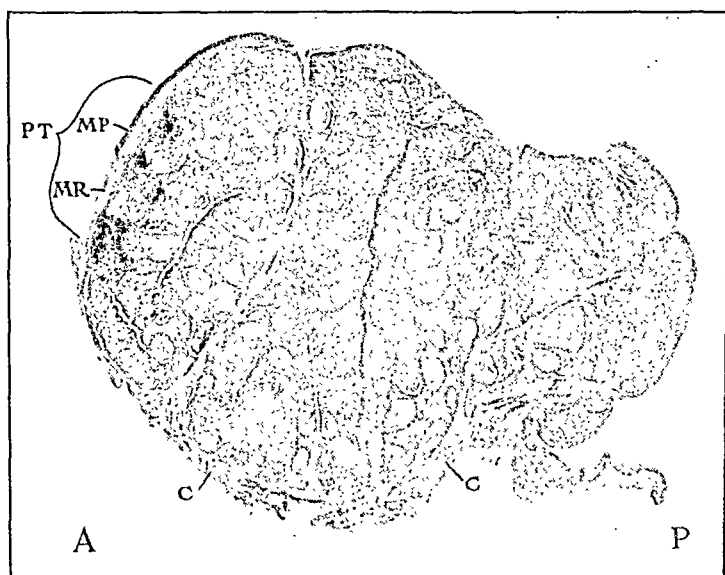


FIG. 6.—Attached plica. Horizontal section of left tonsil viewed from above: *A*, anterior end; *P*, posterior end; *PT*, plica triangularis; *MP*, portion of plica with mucous membrane intact; *MR*, portion of plica from which mucosa was removed at operation; *C*, *C*, capsule.

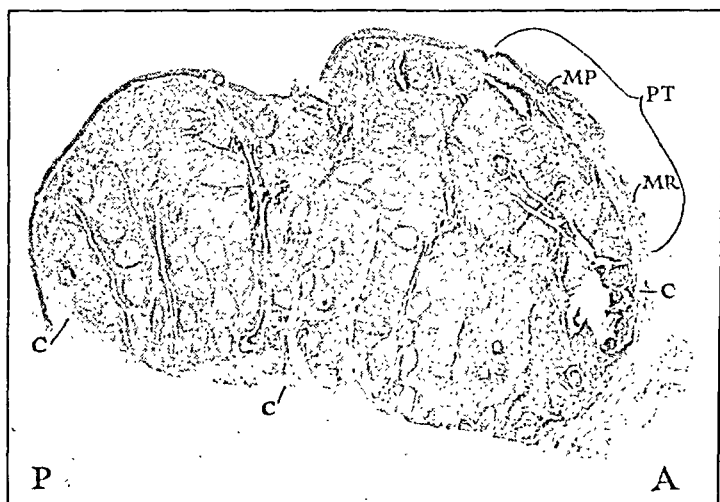


FIG. 7.—Attached plica. Horizontal section of right tonsil viewed from above: *A*, anterior end; *P*, posterior end; *PT*, plica triangularis; *MP*, portion of plica with mucous membrane intact; *MR*, portion of plica from which mucosa was removed at operation.

**THE FREE PLICA AND THE RETROPLICAL OR ANTERIOR TONSILLAR FOSSA.** The term "free" used in this connection is a variable quantity, as merely the edge may be free or there may be quite

an unattached flap which by means of a hook can be drawn laterally and forward, exposing a large surface of tonsil tissue. The latter condition results in the formation of a more or less deep cleft between the tonsil and the plica and gives rise to that form of plica which is usually called unadherent; and it is in this form that drawing outward of the plica by means of a retractor so frequently reveals a crypt or two filled with caseous concretions. This cleft is usually regarded as simply a space lying between the plica and the tonsil and on macroscopic examination this is what it appears to be. The real condition, however, is quite different, as was determined in the following manner. A number of tonsils enucleated from the living were hardened, sectioned horizontally through their equator and then studied microscopically. In quite a few the following state of affairs was found: The plica

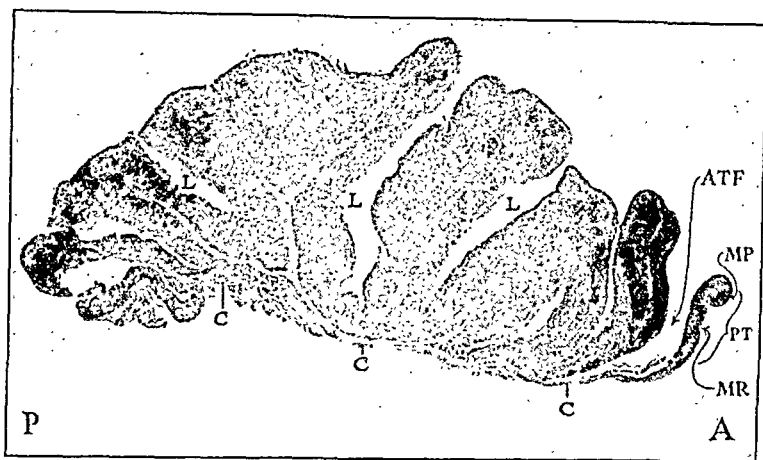


FIG. 8.—Free plica with small anterior tonsillar fossa. Horizontal section of right tonsil viewed from above: A, anterior end; P, posterior end; PT, plica triangularis; MP, portion of plica with mucous membrane intact; MR, portion of plica from which mucosa was removed at operation; ATF, anterior tonsillar fossa; C, C, C, capsule.

was free for a varying distance from its edge. Its buccal surface was covered with mucous membrane which folded around the free margin and lined the superficial part of the anterior boundary of the cleft. Tracing the mucosa toward the bottom of the cleft it was found that it was gradually pushed farther and farther away from the fibrous layer of the plica by a mass of lymphoid tissue which grew thicker the nearer it came to the bottom of the cleft. Around the bottom the lymphoid tissue became continuous with the rest of the tonsil tissue; in other words, the fissure was found to be lined almost throughout by lymphoid tissue (epithelium-covered, of course). It is in reality, therefore, not as is commonly accepted, a space between a fold of mucous membrane and the tonsil, but a large tonsil cleft into which other lacunæ usually empty. To this space the writer ventures to give the name of *anterior tonsillar fossa*

(Figs. 4, 8, 9, and 10) or crypt, on account of its position and evident morphology. The plica, under these architectural conditions, usually fits tightly over the orifices of the secondary lacunæ,

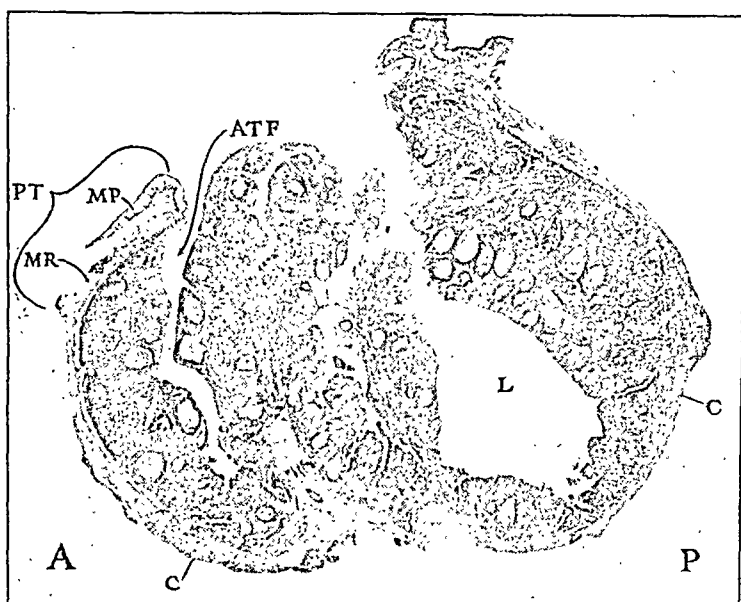


FIG. 9.—Free plica with thick layer of lymphoid tissue and large anterior tonsillar fossa with secondary lacunæ opening into it. Horizontal section of left tonsil viewed from above: *A*, anterior end; *P*, posterior end; *PT*, plica triangularis; *MP*, portion of plica with mucous membrane intact; *MR*, portion of plica from which mucosa was removed at operation; *ATF*, anterior tonsillar fossa; *L*, lacuna; *C*, *C*, capsule.

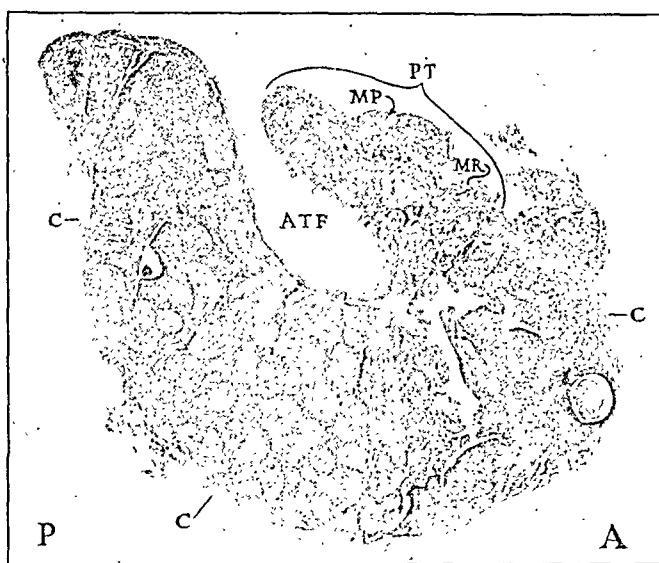


FIG. 10.—Free plica with thick layer of lymphoid tissue and large anterior tonsillar fossa. Horizontal section of right tonsil viewed from above: *A*, anterior end; *P*, posterior end; *PT*, plica triangularis; *MP*, portion of plica with mucous membrane intact; *MR*, portion of plica from which mucosa was removed at operation; *ATF*, anterior tonsillar fossa; *C*, *C*, *C*, capsule.

in this manner preventing ready emptying of their excretions and detritus, and giving rise to that clinical condition called chronic lacunar tonsillitis.

**THE CAPSULAR ELEMENT OF THE PLICA.** This requires no extended description. Sections and dissections of the tonsil show clearly that it is the direct mesial extension of the tonsil capsule beneath the margin of the anterior pillar (Fig. 4), and that the extent of this fibrous element determines the extent of the fold itself. It terminates at the mesial margin of the plica, at which the epithelial layer either passes directly on to the tonsil or else tucks around the edge to cover its deep surface to a varying degree. The same principle applies to the other tonsillar plicæ, namely, that they are extensions of the capsule which project beyond the rim of the tonsil recess and are covered with mucosa on at least one surface. This is shown in the case of the plica retrotonsillaris in Fig. 7.

Hammar,<sup>8</sup> in his splendid study of the ontogeny of the tonsil, attaches so much importance to the plicæ that he bases upon them his classification of the adult gland, as follows: (1) The type in which a plica triangularis has remained, but a plica retrotonsillaris is wanting. (2) The type in which both above-mentioned folds are present, so that the tonsil is hemmed in by a more or less ring-like fold. (3) The type in which only the plica retrotonsillaris is present. (4) The type in which both folds are wanting and the medial tonsillar surface lies wholly in the same surface with the surrounding tissue.

At times, on casual inspection of the throat it is difficult to see where the anterior pillar ends and the plica begins, but firm depression of the side of the tongue will make tense the anterior pillar and define clearly its mesial border. The writer formerly was accustomed to begin his separation of the tonsil by passing a separator down behind the anterior pillar and the plica. This was clearly a gross error for it practically always resulted in an intracapsular operation, since the fibrous or capsule layer of the plica was frequently too strong to be torn through and, therefore, kept the separator back of it. The result was that a more or less thick layer of real tonsil tissue plus capsule was allowed to remain.

#### THE TONSIL.

If the views expressed so far are correct, the tonsil may be defined as follows: The tonsil is a mass of lymphoid tissue, situated in the tonsil recess. Its deep surface is enclosed throughout in a fibrous capsule and its free surface is covered to a greater or

less degree by prolongations of the capsule called plicæ, over which lies a layer of mucous membrane.

With regard to the gross anatomy of this structure many misconceptions exist, as a careful comparison of accepted descriptions with the following will demonstrate.

1. POSITION. When the mouth is closed the tonsil is usually buried, in the sense that it does not project into the buccal cavity beyond the level of the faucial pillars (Fig. 1). Its free surface is concave, probably moulded so by the base of the tongue, and forms a part of the general curve of palate and fauces which ends at the posterior wall of the oropharynx and the base of the tongue.

2. SHAPE. This is usually given as being that of an almond, with an inner and an outer surface, in striking similarity to the old description of the liver, in vogue before the institution of the study of viscera hardened *in situ*. As the result of such study the liver instead of being ascribed an upper and a lower surface is known now to have three in the sagittal plane, an upper, a lower, and a posterior. Likewise, the tonsil has not two, but three well-marked surfaces (Figs. 4 and 5), an antero-internal, a lateral, and a posterior, well separated from each other by definite angles; it approaches in shape more nearly that of a Brazil nut than that of any other conventional figure.

3. SURFACES (Figs. 4 and 5). The antero-internal surface is the one presenting toward the pharynx and the anterior pillar. That portion from the posterior margin as far forward as the anterior pillar, namely, the free portion, is concave, while that which extends forward beneath the anterior pillar is convex. It is studded with lacunar orifices from the line of reflection of the mucous membrane of the plica triangularis on to the tonsil back to the posterior margin of the gland. The lateral surface lies in practically the sagittal plane of the body and is slightly convex. It ends posteriorly where it forms a right angle with the posterior surface. The posterior surface extends inward from the right angle formed at its junction with the lateral. Its median portion is markedly concave on account of being moulded over the thick portion of the palatopharyngeus muscle.

4. POLES (Fig. 5). The upper pole is trifaceted and is buried beneath the palato-glossus at the junction of this muscle with the palato-pharyngeus. The lower pole extends downward, narrowing like the base of a flower petal, and either becomes continuous with the lingual tonsil or fades away on the tongue anterior to the attachment of the epiglottis.

5. ARTERIES. We are told that five arteries supply the tonsil, the facial, the lingual, the internal maxillary, the ascending pharyngeal, and the descending palatine. All of this is interesting, but, nevertheless, utterly valueless from a practical standpoint, as valueless as would be the sole knowledge of the vessels possessed

by a surgeon working on the brain that the latter is supplied by the vertebral and internal carotid arteries. We need to know two things—where to ligate in case of necessity and where the individual arteries enter the tonsil. The list enumerated above affords information on neither point, because the vessels named are intermediate between source and distribution.

As regards a single ultimate source they all receive their blood from the external carotid and this is, therefore, as is well known, the artery which would need to be ligated.

As regards their entrance into the tonsil, there is considerable variation, but the average arrangement is as follows: The writer has ventured to name them according to their position (Fig. 5).

1. THE ANTERIOR TONSILLAR ARTERY OR THE ARTERY OF THE PLICA TRIANGULARIS. This courses up between the mucous and fibrous layers of the plica and breaks up into branches which pierce the fibrous layer to enter the tonsil substance. It is a branch of the dorsalis linguæ and usually is cut at stage 5 of the operation (see below).

2. THE SUPERIOR TONSILLAR ARTERY. This vessel enters the lateral aspect of the upper pole and is a branch of the descending palatine. It is severed necessarily when the velar lobe is lifted from its bed.

3. THE POSTERIOR TONSILLAR ARTERY. This is a small vessel which comes forward through the palato-pharyngeus muscle and enters the tonsil at the angle between the lateral and posterior surfaces, midway between the equator and the lower pole. It is derived from the ascending pharyngeal and is severed during the separation of the tonsil from the posterior pillar.

4. THE INFERIOR TONSILLAR ARTERIES. There are three of these. One runs up the anterior margin, which it enters well below the equator; it is a branch of the dorsalis linguæ. A second runs up the middle of the outer surface in the interval between the capsule and the fossa wall and enters the tonsil a short distance above the equator, at what is sometimes called the hilum. A third enters the middle of the outer surface down near the dorsum of the tongue. The two last mentioned are the largest arteries going to the tonsil and are offshoots from the tonsillar branch of the facial. All three of the inferior arteries are divided at the very end of the operation, namely, when the pedicle is cut.

5. VEINS. The veins of the tonsillar plexus lie in the wall of the recess. The largest vessel of the plexus (Figs. 4 and 20) starts near the upper pole of the tonsil and runs downward along the outer edge of the palato-pharyngeus muscle, opposite the middle of the posterior surface of the tonsil. It is crossed by the glossopharyngeal nerve and then joins with some small veins from the epiglottis and some larger ones from the base of the tongue to form a larger trunk which pierces the superior constrictor at the outer

margin of the palato-pharyngeus muscle; it then empties into the pharyngeal plexus, which lies on the posterior surface of the pharyngeal musculature. A smaller vein (Fig. 4) courses down along the posterior edge of the palato-glossus and empties into one of the lingual veins. In case either of these vessels were torn there would be brisk bleeding from both ends. The larger one is in special danger when sharp instruments are used in separating the tonsil from the posterior wall of the recess, and if by any chance the constrictor were torn, the large veins of the pharyngeal plexus would be injured and the resulting hemorrhage copious. For this reason the region of the posterior pillar should be considered the "dangerous area" in performing an enucleation.

6. FOSSÆ. His<sup>9</sup> was the first to name the fossa supratonsillaris, and according to the state of knowledge at that time his term was correct. It is now recognized, as pointed out by Fraser,<sup>10</sup> that this fossa is within the tonsil, since it lies below the upper part of the capsule as well as below a layer of lymphoid tissue of varying thickness. A better term for it would be the upper or *superior tonsillar fossa*, as indicating its position and real morphology and as opposed to the anterior tonsillar fossa described above.

7. THE POSTERIOR FAUCIAL PILLAR is fundamentally the palato-pharyngeus muscle with mucous membrane covering that portion of it which projects mesially beyond the tonsil and its capsule. The upper part, which curves over to the uvula, usually is without muscle tissue. With a large tonsil only the mesial edge of the pillar is visible, while with a small one much more of the pillar can be seen. When the posterior part of the capsule projects into the throat and is free of the pillar, the resulting fold is the plica retrotonsillaris.

8. THE PALATO-PHARYNGEUS MUSCLE. This muscle arises in the soft palate and from the Eustachean cartilage, its upper mesial portion, that arising from the tubal cartilage being covered by the mucosa of the salpingopalatine fold. It passes downward and slightly inward behind the tonsil to blend in its lower part with the musculature of the pharynx and to be inserted into the posterior border of the thyroid cartilage. From a point opposite the upper pole of the tonsil, where with the mouth closed it is crossed at almost a right angle by the palato-glossus, down to about the equator of the tonsil, its posterior surface is free from the other muscles and a probe can be passed back of it with freedom. In this part of its course, the muscle is narrow from side to side and thick from before backward, its anterior edge forming a well-marked anterior projection (Figs. 4 and 20). Overlying it in this situation is the mesial portion of the posterior surface of the tonsil, which is notably grooved by the muscle.

<sup>9</sup> Loc. cit.

<sup>10</sup> Loc. cit.



From the equator of the tonsil down, the muscle begins to flatten and spread out fan-wise until at its lower part, opposite the epiglottis the prominent anteriorly directed ridge has faded away entirely. Throughout all of the lateral margin which presents in the tonsil recess, as far down as the base of the tongue, runs the largest vein of the tonsillar plexus. Coming forward through the substance of the palato-pharyngeus muscle can be seen the posterior tonsillar artery.

#### THE PRINCIPLES OF TONSIL ENUCLEATION.

1. All tissue evidently diseased should be removed.
2. All tissue possibly diseased or likely to become so should be removed, provided the life of the patient is not endangered thereby. This applies with particular emphasis to tuberculous and malignant disease.
3. To include all tonsil tissue in the operation, extracapsular enucleation must be performed.
4. Conversely, any operative procedure which fails to remove the capsule is certain to allow some tonsil tissue to remain in place.
5. The plane of operation should be between the capsule of the tonsil and the wall of the tonsil recess.
6. The first step in the operation should be the entrance into the proper tissue plane by the most certain and the most accessible route. This route, if possible, always should be the same.
7. Having reached the proper tissue plane every endeavor should be made to remain there.
8. For this reason, the bluntest possible instruments should be used and sharp ones avoided, as the latter may deviate either into the tonsillar parenchyma or into the wall of the tonsil recess.
9. The most difficult portion to dislodge is the upper lobe and hence, this part should be made certain of as early as possible.
10. The portion first to be attacked should be that having the minimum of direct blood supply, in order that subsequent step should be obscured by blood to the least possible extent. The anterior and upper portions meet this requirement, as the main vessels enter below the equator.
11. The vessels entering and leaving the tonsil are bound to be severed, and therefore, they should be divided by the method best calculated to promote quick clotting, namely, divulsion by some blunt separator.
12. Care should be taken to avoid lacerating the wall of the tonsil recess, for two reasons. The first is that in it lies the tonsillar venous plexus, injury to which, in the writer's experience, is the most common cause of serious hemorrhage. Another reason is that laceration of the palatal muscles will cause the formation of

cicatrices and possibly interference with normal phonatory movements, as pointed out by Makuen.<sup>11</sup> Particular care should be taken to prevent wounding the palato-pharyngeus, although this may be over-emphasized, as the writer has seen cases of marked cicatricial deformity of the palate with no interference with function.

13. To avoid lacerating the muscles lining the recess the loosening of the tonsil should be done in lines parallel with the muscle fibers. In the lateral wall is the superior constrictor whose fibers run horizontally and in the posterior wall is the palatopharyngeus whose fibers run vertically. The lateral aspect of the tonsil, therefore, should be freed by horizontal movements and the posterior aspect by vertical.

14. The "dangerous area" is the posterior wall of the tonsil recess, since injury to it would result in wounding of the largest vein of the tonsillar plexus, tearing of the palato-pharyngeus muscle, and, if the latter and the superior constrictor were perforated, lacerating of the pharyngeal venous plexus.

15. The main vessels of the tonsil enter its base and hence the stump should be severed by an instrument best calculated to close the divided vessels. For this purpose scissors, knife, and guillotine are inferior to the snare.

16. The possibility of the patient's being a hemophiliac should always be considered and if the history is strongly suggestive, operation had better be refused. The clotting time of the blood may be taken and the effect of calcium or thyroid feeding tested. If the time can be brought down to five minutes or less operation may be done.

17. Serious postoperative hemorrhage is usually caused by one of three things: (a) Injury of the tonsillar or the pharyngeal venous plexus, which can be avoided by using no sharp instrument; (b) leaving a fragment of tonsil tissue in place,<sup>12</sup> and (c) failing to remove the capsule. The last two conditions mentioned both cause this effect by holding open and preventing the collapse of the tonsil recess. The capsule maintains the integrity of the fossa and braces it open, as the old-fashioned hoop kept the skirt spread wide, or the ribs of an open umbrella keep it stretched. Remove the hoop or ribs and the soft material would collapse; likewise remove the capsule and the fossa contracts. This is proved by the post-operative results of extracapsular enucleation. After the capsule is removed the ends of the vessels all lie in soft muscle tissue, in which they can easily contract and retract. If the capsule is allowed to remain, it is probable that each vessel mouth is held in a ring of fibrous tissue, and Nature's method of closing torn vessels is interfered with.

<sup>11</sup> New York Med. Jour., August 5, 1911.

<sup>12</sup> Turner, Logan, Transactions of the Medico-Chirurgical Society of Edinburgh, 1910-1911, p. 69.

18. A fair conclusion would seem to be that enucleation, with prohibition laid on all sharp instruments, is the safest, as well as the most effective, method of operating.

#### THE PRACTICE OF TONSIL ENUCLEATION.

The secret of a clean and thorough enucleation is to get at once to the outer surface of the capsule and to stick close to it through the remainder of the operation. The getting there is easy, provided the anterior relations of the tonsil are thoroughly appreciated, and the staying there is equally easy as well as safe, if no sharp instruments are used. Success lies in understanding the significance of and making proper use of the plica triangularis, and in the correct interpretation and proper surgical treatment of this little structure resides the crux of the whole operation. Whatever its condition, free or attached, its anterior facies should be regarded as the portal of entry for the enucleating instruments. If the mucosa, and only the mucosa, of the former is removed, the operator is at once at the outer surface of the capsule and the only remaining problem is to follow it outward, upward, and backward and then downward, and the tonsil and capsule will be found to be completely freed except at the base. A successful outcome depends mainly upon making a correct start, and this necessitates getting into the proper tissue plane, namely, that between the tonsillar capsule and the fossa wall. If one does so, the rest is easy; if one does not, a ghastly mess is the result, since to attempt to make a clean enucleation within the confines of the capsule is too harassing a procedure to view with anything but vexation and to result in anything but failure.

The operation, as the writer has worked it out for his own use, is detailed herewith, an attempt having been made to divide it into stages and to give the reasons for each and every maneuver. There is no intention of claiming superiority of method; the endeavor of the writer has been simply to apply to the practice the principles previously enumerated, and to put on an anatomical basis an operation about which so many divergent views are expressed.

**PLACE OF OPERATING.** This is invariably a hospital. The operation is distinctly not a minor one and the operator needs to be surrounded by all favoring facilities, which would include proper sterilization of everything used, adequate illumination, apparatus for meeting any emergency, either at or following the operation, and trained watching of the patient subsequent to the operation. If the patient is not allowed to go to a hospital the writer refuses to operate.

**PREPARATION OF THE PATIENT.** The patient reports at the hospital late in the afternoon of the day preceding the operation,

A light supper is given, following which the patient goes to bed and is given a dose of castor oil. In the morning an enema is given if the bowels do not move spontaneously. An enema is always given just before the patient is taken to the etherizing room. Either no breakfast or a cup of milk or clear bouillon is given about eight o'clock, the former if the operation is to be in the morning, the latter if in the afternoon. The patient is kept in bed until the time of operation and the nose sprayed every hour with potassium permanganate solution, 1 to 10,000.

**ANESTHETIC.** Ether, unless contraindicated.

**POSITION OF PATIENT.** Supine, with the head raised on a small hard pillow and turned slightly toward the right.

**POSITION OF OPERATOR.** At the right of the patient.

**POSITION OF ANESTHETIST.** At the head of the table.

**DUTIES OF ANESTHETIST.** To administer the anesthetic, to hold the mouth gag in place and to move the patient's head at the direction of the operator. The terms the writer uses are "flex," "extend," "rotate right," and "rotate left."

**POSITION OF ASSISTANT.** At the left of the patient.

**POSITION OF INSTRUMENT TABLE.** At the left hand of the operator.

**POSITION OF ASSISTING NURSE.** Behind instrument table.

**DUTIES OF NURSE.** To keep instruments clean and in order and to keep gauze carriers armed with gauze.

**ORDER OF OPERATION.** Right tonsil, left tonsil, adenoids.

**INSTRUMENTS.** Mouth gag, tongue depressor, two self-retaining tonsil forceps, Myles' punch, Quicksall's tonsil dissector, snare, six sponge holders, La Force adenotome, Wood's pillar retractor.

**SPONGES.** (1) Small gauze sponges folded tight and carried in long sponge holders. (2) "Fluff"—long loose strips of gauze.

**THE OPERATION ITSELF.** This consists of two parts, the freeing of the tonsil and the cutting through of the pedicle.

**STAGES OF THE OPERATION.** 1. Insert the mouth gag, and if it is of the lateral type, place it on the patient's left side. Have the ends covered with rubber tubing to protect the teeth.

2. Insert the tongue depressor and press the tongue downward sufficiently to make clear the mesial border of the anterior pillar. This will aid in locating the limits of the plica triangularis.

3. Grasp the tonsil at its middle with a pair of forceps and draw it toward the median line (Fig. 11). This defines and makes tense the plica triangularis and renders more easy stage 5.

4. Transfer the tongue depressor to the assistant, who takes it in his left hand. The whole attention of the assistant should be concentrated upon holding the depressor in the correct position.

5. With the Myles punch snip out a strip of the mucous membrane of the plica triangularis just internal to and parallel with the anterior margin of the anterior faucial pillar, beginning below

and working upward (Fig. 12). If this is done correctly there is exposed a linear area of capsule, in the shape of the lateral margin of the plica. The writer regards this as the *sine qua non* of the entire procedure. Of all instruments, the punch is given the preference because with it the snipping of mucous membrane only

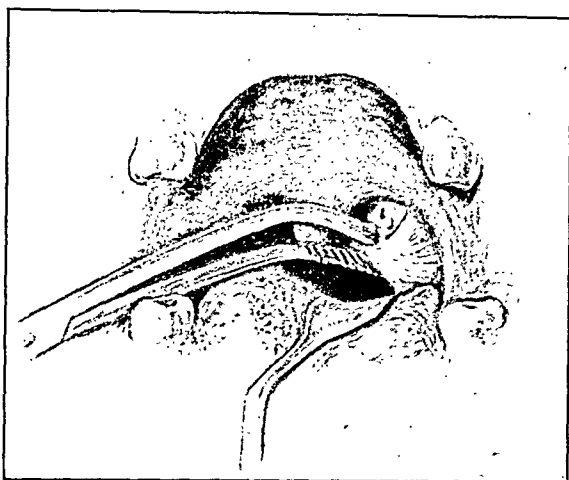


FIG. 11.—Plica triangularis made tense by median traction on the forceps.



FIG. 12.—A strip of the mucous membrane of the plica triangularis snipped out by the punch, exposing the capsular element of the plica.

is so readily performed. A fatal error at this point is to go through the fibrous layer of the plica, for then it is no longer possible to do an extracapsular operation, and once inside the capsule it is an extremely difficult matter to get outside again.

If an ordinary knife or a pair of scissors, as recommended by many, are used at this stage it is very easy to make the incision

too deep and pass through all of the plica into the parenchyma of the tonsil.

A small vessel, the anterior tonsillar artery, usually is cut at this stage of the operation.

6. With the Quicksall dissector placed in the groove cut in the mucous membrane push laterally the anterior pillar of the fauces (Fig. 13). This instrument is used because while not sharp it

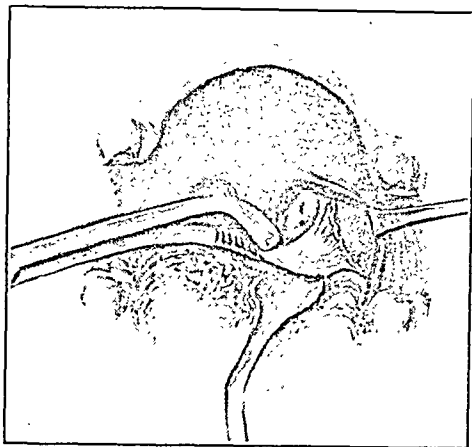


FIG. 13.—The anterior angle of the tonsil exposed by pushing aside the anterior pillar.

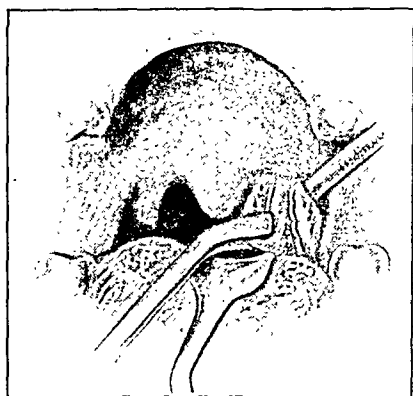


FIG. 14.—Insertion of the blunt separator at the anterior angle of the tonsil preliminary to freeing the upper pole of the tonsil.

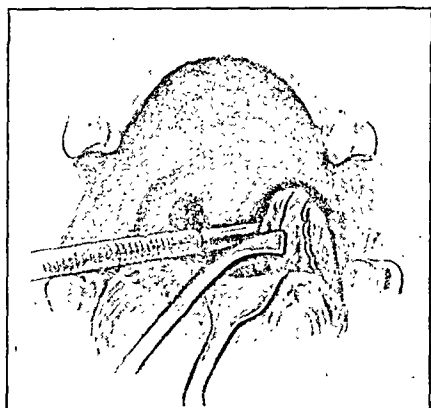


FIG. 15.—The freeing of the upper pole completed.

has sufficient of an edge to engage a layer of mucous membrane. The pillar is pushed away because it overhangs the anterior margin of the tonsil and to lift the latter from its bed, it is essential to reach the outer surface. This can be most quickly and most handily done at its anterior angle, namely, that beneath the palatoglossus muscle.

7. Into the opening thus produced insert some pointed but very blunt dissector (Fig. 14), such as the straight end of an Allis

dissector, which is somewhat too broad to be entirely satisfactory. The instrument now lies between the capsule and the anterior pillar and unless the end is shoved into the surrounding tissues with much force it will remain automatically in the correct plane.

8. With a firm sweep of the blunt dissector first upward, then backward, and finally downward and inward, deliver the upper pole of the tonsil into the pharynx (Fig. 15). This not only frees the velar lobe from the deep connections of the capsule but also

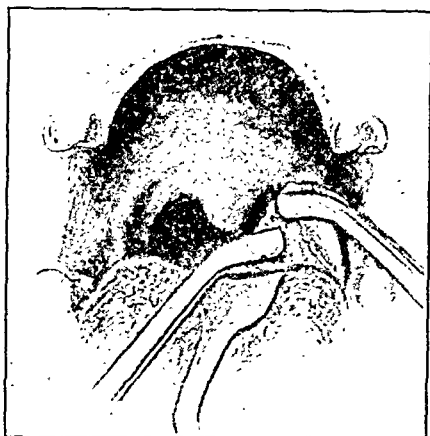


FIG. 16.—The application of the second pair of forceps.

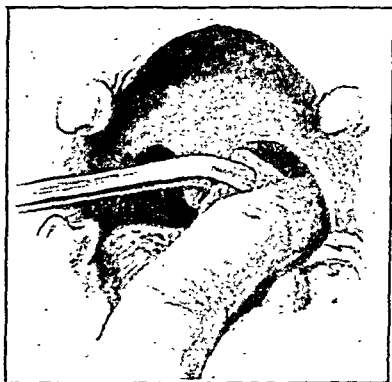


FIG. 17.—The freeing of the lateral aspect of the tonsil.

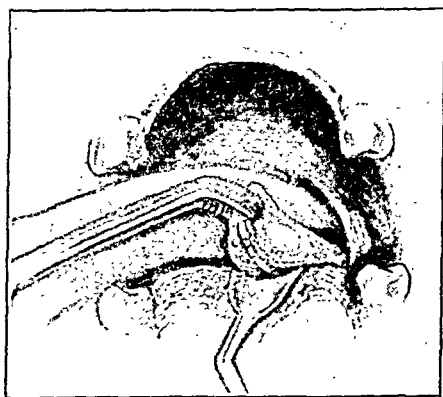


FIG. 18.—The freeing of the posterior aspect of the tonsil.

divides the mucosa which is reflected from the soft palate and the upper part of the posterior pillar on to the tonsil. It is the second of the two most important maneuvers of the operation, since it enucleates the most buried part of the tonsil and allows of its being grasped and drawn into the throat sufficiently far to permit of the subsequent manipulations.

9. Grasp the upper pole of the tonsil with a second pair of forceps (Fig. 16); these should be so constructed that the loop

of a snare can be slipped over the handles. The Kaufman model has been satisfactory in every way. One blade should be applied to the buccal and the other to the capsular or deep surface and sufficient tissue always should be included to give a firm hold and prevent slipping; if the grip is lost it is difficult sometimes to secure a second one. The attaching of the forceps to the upper pole can be done easily, since the velar lobe has been freed; it can be facilitated by median traction of the forceps first applied.

This step is a most essential one since with a forceps attached at this point the loosened portion of the tonsil can be drawn toward the median line and the area between the freed part and its bed materially widened. It also allows of the stretching upward of the tonsil, thus increasing its firmness and facilitating subsequent digital dissection.

10. Remove the first pair of forceps. They have served their purpose and would be in the way from now on.

11. Drawing the tonsil inward and upward by means of the forceps, sweep the index finger around the tonsil, freeing it from its attachments everywhere except at the very base, using the finger of that hand which experience shows to be the more convenient (Figs. 17 and 18). In performing this separation the finger should move in the directions of the adjacent muscle bundles, to avoid as far as possible tearing any of them. In the lateral wall of the fossa is the superior constrictor, and in the posterior wall is the palato-pharyngeus. As the fibers of the former run in a horizontal direction, and those of the latter in a vertical, the movements of the enucleating finger should be governed accordingly. The finger at this stage is a most reliable instrument as it not only does the separating quickly and thoroughly, but also is so blunt that it does not get out of the correct tissue interval. In addition it is furnishing to the operator information as to how the separation is progressing. It has the advantages also of doing away with the necessity of sponging and watching the operation field, since its work can be done entirely by touch; thus much time is saved. While it may be true, as Lothrop<sup>13</sup> states, that the pain after tonsillectomy is most severe in those cases in which the finger has been used, the difference is negligible.

The writer does not believe in the possibility of doing the entire operation with the finger, as is advocated by some, as there would be too great chances of getting inside the plica and digging out the lymphoid tissue only, leaving the capsule.

12. Have the assistant remove the tongue depressor, as it is of no further use.

13. Sever the base of the tonsil by means of a snare (Fig. 19). This instrument is chosen for two reasons, one being that it crushes

<sup>13</sup> J. S. Fraser, loc. cit., p. 163.



the vessels, thus promoting hemostasis, the other being that it adjusts itself to the shape, size, and position of the stump. As the latter is conical, with the base upward, the chances are that it will be directed automatically to the very narrowest part before it begins to cut. Two precautions should be observed in using the snare, one being that the loop on introduction is not too large, a fault which results frequently in leaving a stump of tonsil tissue, the other being that the loop should be palpated before being tightened, in order to determine that it is exactly in the proper place.

There is really no reason why there should be any controversy as to the efficacy of guillotine and snare. In the writer's opinion neither should be used for the operation proper, their correct sphere being simply to sever the pedicle and for this purpose the snare certainly is more efficient.

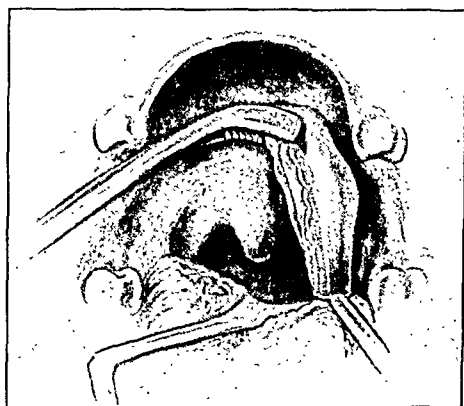


FIG. 19.—The application of the snare to the pedicle.

14. Hold a pledget of gauze in the fossa for a moment and then remove it.

15. Retract the anterior pillar and look for points of hemorrhage. If everything is safe, proceed to the other side. At this stage usually it will be found necessary to administer more of the anesthetic.

AFTER-TREATMENT. 1. The patient stays in bed the remainder of the day.

2. The patient is kept on the side until well out of the anesthetic. If there is any bleeding the blood will run out of the mouth with the patient in the lateral position. If the dorsal position is occupied, blood may trickle down the esophagus, without being noticed by either nurse or patient. Blood can flow down the esophagus without deglutition, as the writer knows to his sorrow.

3. Cracked ice is allowed as soon as thirst is complained of. No treatment is given to the nose or throat.

4. Soft and preferably very hot or very cold food is allowed five hours after the patient arrives in his room.

5. If temperature, pulse, and respiration are normal, the patient is allowed to be up the morning after operation and to go home in the afternoon, going at once to bed.

6. The following day the patient is out of bed, but in the house all day.

7. The third day after operation the patient goes about his usual routine.

#### CONCLUSIONS.

**EFFICIENCY.** In about 200 operations with the above technique, the writer has succeeded in removing all of each tonsil with but two or three exceptions. The latter have been cases in which digital dissection was not carried down far enough, and a stump was allowed to remain in the lower part of the tonsil recess.

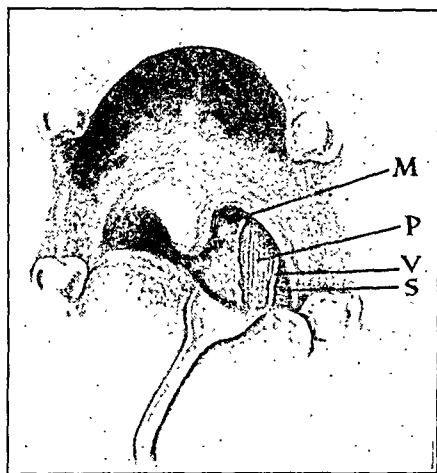


FIG. 20.—The fossa after removal of the tonsil: *P*, palato-pharyngeus; *S*, superior constrictor; *M*, mucous membrane of the posterior pillar; *V*, largest vein of tonsillar plexus.

**SAFETY.** In not a single case has there been any serious or even alarming hemorrhage. This probably is due to the fact that the peritonsillar vessels were not injured and that the tonsillar vessels were severed in a way most likely to promote closure. In addition the removal of the capsule allowed the fossa to contract and thus aid in occluding the cut vessels.

**EASE.** The operation is readily performed, as it is always done with the same technique and from the time the velar lobe is freed the succeeding steps can be done by sense of touch alone. This avoids frequent sponging and thus materially shortens the time required.

**RESULTS.** Usually the immediate result (Fig. 20) is a large recess filled with frothy saliva and lined with the usual mem-

brane. This is replaced later by more or less granulation tissue, and ultimately the anterior pillar largely, if not entirely, fades away into the lateral wall. No undesirable vocal effects have been noted. The verdict of singers has been that the resulting voice is "bigger." If the posterior pillar were lacerated, the resulting cicatrices might be deleterious, but the writer has been fortunate enough to escape inflicting such injuries.

The writer wishes to express his indebtedness to Drs. George A. Piersol, Paul A. Lewis, W. H. F. Addison, and P. G. Skillern, Jr., for their aid in the preparation of this paper.

---

### CHVOSTEK'S SIGN AND ITS SIGNIFICANCE IN OLDER CHILDREN.

BY MURRAY H. BASS, M.D.,

ATTENDING PHYSICIAN, CHILDREN'S DEPARTMENT, MT. SINAI HOSPITAL DISPENSARY,  
NEW YORK CITY.

IN 1876 Chvostek, of Vienna, described a sign which he believed was characteristic of tetany. The sign, which since that time has been called Chvostek's sign, or the facial phenomenon, consists in an easily demonstrated mechanical excitability of the peripheral nerves. By tapping either with the finger or a percussion hammer on the skin over the facial nerve, that is, at a point about midway between the zygoma and the angle of the mouth, one obtains when the sign is present, a lightning-like contraction of the muscles supplied by the facial nerve; the angle of the mouth, the side of the nose, and in marked cases the skin over the inner canthus of the eye and eyebrow display a sudden twitching.

There has been some dispute as to the cause of the twitching, some authorities claiming that it was due to a spinal reflex, others that it was merely a heightened irritability of the nerve trunk. Escherich,<sup>1</sup> in a rather ingenious manner, adds weight to the latter hypothesis by the following experiment: By applying a 10 per cent. cocaine solution to the skin, then using kataphoresis, he anesthetizes the skin over the cheek; on tapping this area the phenomenon nevertheless remains positive. On the other hand when the skin over the inner surface of the thigh is thus anesthetized the cremasteric reflex cannot be obtained. He therefore is inclined to disregard the reflex theory and to consider the twitching due to direct stimulation of the overexcitable facial nerve trunk.

At first it was supposed that this symptom was present only

<sup>1</sup> Die Tetanie der Kinder, Vienna, 1909.

in individuals suffering from tetany, and indeed to this day it is universally regarded as one of the three cardinal signs of that disease, the other two being Trousseau's and Erb's. Chvostek's sign is so easily elicited and so characteristic that it has been tried for in many varied conditions exclusive of tetany, and numerous observers have found it present in conditions which seem to have nothing at all to do with that disease. Not only is the constancy of the sign questioned, but the degree to which the face twitches has been interpreted as being of varied importance. Schlesinger<sup>2</sup> divided the phenomenon into three grades, designated types 1, 2, and 3, according as the twitching was confined to the scarlet border of the lip, the side of the nose, or the entire side of the face. All the observers, including Chvostek, attach little or no importance to the twitching of the scarlet border of the lip alone. The most marked facial twitching, that is, type 3, is by many conceded to be present only in tetany. It is only in tetany also that the so-called Schultz phenomenon is observed, that is, where there is such increased excitability of the nerve that by merely lightly stroking the skin a distinct facial twitching may be obtained.

It is rather difficult to gather statistics about this subject from the literature, for (1) there is no unanimity as to the method of classifying the types of the reaction, (2) most of the work has been done on adults, and (3) we are not yet sure whether infantile and adult tetany are identical, especially since what is generally conceded to be a criterion in infants, that is to say, Erb's electrical reaction, has not been sufficiently investigated in young adults for one to know the positive normal figures. The occurrence of the sign during infancy, however, has been usually considered as positive evidence of tetany, although the electrical reaction (heightened galvanic irritability) is a more delicate test, and often shows latent tetany when Chvostek's sign is negative. The sign has been found positive by German investigators especially frequently in older children, and these positive cases have been variously interpreted as latent tetany, as cases of neuropathic diathesis, or the positive sign has been considered simply as a chance find of no diagnostic significance whatever.

In view of the fact that tetany occurs more rarely in America than in Europe, and especially than in Austria, where most of the previous investigations along this line have been carried out, it seemed of interest to obtain figures concerning the occurrence of the facial phenomenon in children attending American clinics, for it seemed logical to conclude that if the phenomenon was positive in as large a number of cases here as abroad, where the distribution of tetany is so different, the isolated facial phenomenon would seem to have no dependence on present or previously existing tetany.

<sup>2</sup> Zeitschr. f. klin. Med., 1891, xix, 487; Wien. klin. Woch., 1910, p. 315.

Among the observers who believe the sign to be pathognomonic of tetany is Chvostek, Jr.,<sup>3</sup> of Vienna. From time to time in the past few years he has published numerous studies on the subject, and especially in an article published in 1907,<sup>4</sup> lays great stress on the importance of the sign. In 840 cases of illness in adults only 6 cases had a positive facial of type 2 or 3, in which no sign or history of tetany could be obtained. In all the other cases in which it was present, distinct signs of tetany manifest or latent were found. The more intense the degree of facial present the more likely was the case to be one of tetany. Chvostek concludes his article as follows: "We believe that the mechanical hyperexcitability of the nerves, especially the facial, is an easily elicited and important symptom of diseases of the parathyroids, a delicate test which reveals to us a disturbance in the functions of these organs."

Frankl-Hochwart,<sup>5</sup> writing on tetany in Nothnagel's *System*, does not go so far as this. He believes that the isolated facial phenomenon (by which is understood a positive Chvostek's sign without any other sign of tetany) may at times mean tetany; but that there are surely many cases in which it has nothing at all to do with that disease. However, he brings out an interesting point which connects the sign more intimately with tetany, namely, that in those years in which tetany was epidemic in Vienna there appeared in persons ill with other diseases, a much greater number of positive facials, and conversely in those years in which there was little tetany to be seen in Vienna, few patients suffering from other diseases showed the sign. Furthermore, to show the connection between the facial and tetany, he examined a series of cases of tetany a number of years after the attack, with the following results: In chronic and relapsing cases Chvostek's sign was present in every instance (7 cases); in 19 cases where only paresthesias remained the sign was absent only five times; in 6 cases which had lost all symptoms but general debility and weakness it was present twice; in those cases which were entirely cured, 5 in number, the sign was negative in all.

In 1891 Loos,<sup>6</sup> in Vienna, came to the conclusion after the examination of a large number of cases that the sign was present not only in tetany but in many other diseases as well, and that it was frequently found positive in hysterical and nervous children. He describes 80 children with positive facial phenomena, but without any other signs of tetany. The children were suffering from various diseases and did not show hyperirritability of any other muscle groups. He concludes that: (1) The positive sign in some cases is an

<sup>3</sup> Wien. klin. Woch., 1905, No. 38; Deut. med. Woch., 1909, p. 825; Zeitschr. f. klin. Med., 1891, xix, 489.

<sup>4</sup> Wien. klin. Woch., 1907, No. 17.

<sup>6</sup> Wien. klin. Woch., 1891, No. 49.

<sup>5</sup> Tetanie, in Nothnagel's *System*.

expression of general disturbance of nutrition. (2) It may be present in a number of members of the same family, where it is an expression of a heightened irritability of the nervous system. (3) It may be present in tetany.

Oscar Herbst,<sup>7</sup> in Berlin, in 1910, published an examination of 500 school children, among whom he found the sign most often in the fourteenth year. It was present in 43 per cent. of the children, and was marked in 18 per cent. He does not attach much importance to the sign.

Sperk,<sup>8</sup> also writing in 1910, concludes that the isolated facial is rare in infancy, and that it increases rapidly from the fifth to the fourteenth year. He also points out that the sign when present in older children occurs in nervous individuals who have increased knee-jerks and diminished corneal and pharyngeal reflexes. He believes that it is a helpful sign when found in conjunction with others in making the diagnosis of a neuropathic child.

Thiemich,<sup>9</sup> on the other hand, is opposed to this view and clings to the belief that the sign is pathognomonic of tetany even when present in older children without any other signs. He has observed a number of children who showed the sign in infancy when they had typical tetany. The sign then disappeared, to return again later on, after the fifth year, without being accompanied by any other manifestations of tetany. His conclusions read: "The facial must be stricken from the list of nervous stigmas and must be regarded even in late childhood as a pathognomonic sign of latent tetany, even if this disease remains continuously a symptomless anomaly of the nervous system."

Lust,<sup>10</sup> in 1911, before describing a new sign which he believes is present in 97 per cent. of cases of spasmophilia, that is, eversion of the feet when the skin is tapped upon over the external popliteal nerve as it winds around the head of the fibula, summarizes the various viewpoints concerning the significance of Chvostek's sign. He concludes that in infancy its occurrence has a distinctly pathological significance, that it means tetany, but that it is present in only about 50 per cent. of cases of this disease. He examined 40 spasmophilic children of all ages and found the sign present in 45 per cent. and absent in 55 per cent. Of the babies, 34 in number, 15 had positive facials (44 per cent.) and 19 had none (55.9 per cent.). An absent facial in infants does not exclude spasmophilia, for in latent tetany as the child improves the sign disappears before the electrical reaction becomes normal.

The latest contribution on the subject is by Hochsinger.<sup>11</sup> He has examined all the children of his private practice for many

<sup>7</sup> Deut. med. Woch., 1910, No. 12.

<sup>8</sup> Wien. klin. Woch., 1910, No. 5.

<sup>9</sup> Monats. f. Kinderheilkunde, 1902, No. 3: Tetany, in Pfaundler and Schlossman's System.

<sup>10</sup> Munch. med. Woch., August 8, 1911.

<sup>11</sup> Wien. klin. Woch., October 26, 1911.

years past, for the presence of this symptom, and comes to the conclusion that apart from its significance in tetany it is useful as a sign of a neuropathic constitution in childhood. He finds Chvostek's sign frequently present in the mothers, less often in the fathers of the children showing it, thus emphasizing the hereditary character of nervous stigmas. Of 117 children showing symptoms of nervousness, 101 showed the sign, 26 of these were generally nervous, without any special symptoms, the other 75 showed pavor nocturnus, migraine, nervous anorexia, enuresis, etc. Of the mothers of these children 61 showed positive facials. The sign disappears in boys at about the sixteenth year; in girls, on the other hand, it may remain to the thirtieth year, frequently not disappearing until the menopause. The sign may disappear in summer to return again during the cold weather. When present in normal children he could always find neurotic antecedents. His conclusions are: "The isolated facial in older children has in all cases a pathological significance. The facial is one of the chief symptoms of over-excitability and nervousness in youth, and seems to be more deeply rooted in the female than in the male sex. Juvenile nervousness and infantile hyperexcitability (that is, spasmophilia of infants), belong genetically together, and depend ultimately on hereditary neuropathic tendencies."

During the past summer I noted that in older children applying for treatment at my clinic at Mt. Sinai Hospital Dispensary the presence of this sign was by no means a rare occurrence, and therefore in the months of September, October, November, and December every new case was tested for the presence or the absence of the sign. In all 495 children, ranging in ages up to fourteen years, were examined. It was positive in 16 of these cases, that is, 3.2 per cent. The percentage at the different ages can be seen in Table I. It will be noted that the sign is present only in 1 per cent. of the children aged under three years, and then becomes gradually more frequent until it reaches 19.6 per cent. in children aged ten to fourteen years. These figures agree fairly well with those found by German observers.

TABLE I.—Ages at which Chvostek's Sign was Found in Examining 495 Children. Sixteen Positive Cases.

Age.	1 to 3 years.	4 to 6 years.	7 to 9 years.	10 to 14 years.
Males . . . .	102	32	23	24
Females . . . .	107	37	33	27
	} 209		} 56	
	} 69		} 51	
Positive cases . . .	2	2	2	10
Percentage . . . .	1 per cent.	2.9 per cent.	3.6 per cent.	19.6 per cent.

Analyzing my series of cases to see how far the positive Chvostek means tetany, I must conclude that there seems to be no case

among these 16 (nor among the 15 to be described later) in which a positive diagnosis of tetany, present or previous, could be made. In only 2 of the cases (Cases I and XV) could a history of convulsions be obtained. In the one case a girl, aged fifteen years, had had a number of general convulsions when aged eight to nine years, but since then she has had no more. Although she had a marked Chvostek's sign, her electrical reaction to galvanism was normal. Her brother (Case XVI, Table III) also had never been sick, except for his present complaints of nervousness and headache. Both the children showed orthostatic albuminuria.

TABLE II.—Analysis of Thirty-one Positive Cases (Thirteen Males and Eighteen Females).

Case No.	Age (years).	Sex.	Degree of twitching.	Diagnosis.
I	6	M.	3	Hysteria.
II	14	F.	2	Headache.
III	10	F.	1	Headache.
IV	12	F.	1	Neurotic.
V	13	M.	3	Neurotic.
VI	10	F.	1	Neurotic.
VII	12	F.	3	Neurotic.
VIII	12	F.	2	Neurotic.
IX	12	F.	1	Orthostatic albuminuria.
X	13	M.	1	Orthostatic albuminuria.
XI	5	F.	1	Orthostatic albuminuria.
XII	11	F.	3	Orthostatic albuminuria.
XIII	7	F.	2	Orthostatic albuminuria.
XIV	12	F.	2	Orthostatic albuminuria.
XV	15	F.	3	Orthostatic albuminuria.
XVI	13	M.	1	Orthostatic albuminuria.
XVII	11	M.	2	Orthostatic albuminuria.
XVIII	13	F.	3	Orthostatic albuminuria.
XIX	10	M.	2	Orthostatic albuminuria.
XX	11	F.	3	Orthostatic albuminuria.
XXI	13	F.	3	Orthostatic albuminuria.
XXII	6	F.	2	Bronchitis.
XXIII	2	F.	2	Bronchitis.
XXIV	1½	M.	3	Bronchitis.
XXV	9	M.	3	Bronchitis.
XXVI	12	M.	1	Bronchitis.
XXVII	8	F.	1	Hypertrophied tonsils.
XXVIII	9	M.	3	Asthma.
XXIX	12	M.	3	Enuresis.
XXX	14	M.	3	Mitral stenosis.
XXXI	9	M.	3	Cyclic vomiting.

The second case giving a previous history of convulsions (Case I, Table II) was a boy, aged six years, who for a year had been subject to peculiar attacks, resembling Jacksonian epilepsy. Chvostek's sign in his case was also well marked but his electrical reactions were normal, and the diagnosis of late tetany (tetanoid späteklampsie of Thiemich) was therefore ruled out. He showed signs of hysteria, such as temporary deafness, irregular and varying areas of anesthesia, and analgesia and was therefore classed as a



case of hysteria. An interesting observation was made in this case as regards the variability of Chvostek's sign. The child was seen one afternoon and showed a very strongly marked facial phenomenon. A few days later he had convulsions followed by several hours of coma. After regaining consciousness Chvostek's sign could not be obtained. Stoeltzner<sup>12</sup> reports a similar case of the disappearance of the sign directly after a convulsion in an infant suffering from tetany.

Excepting in these 2 cases of convulsions mentioned above no history of any symptoms of tetany, such as laryngismus or carpopedal spasm, could be obtained in any of the cases. In a few children electrical irritability was tested, but no case showed galvanic hyperirritability. It seems fair then to conclude that these cases with the possible exception of Case XXVIII, are not cases of latent tetany.

The next question to be considered is whether these cases showing the positive sign in any way resemble each other; whether they fall into any well-defined group. I think that this can be answered in the affirmative by a consideration of Table II, which shows the diagnosis or chief complaints of children in my own series in whom the sign was positive. It will be noted that there are 15 more cases than in Table I. These were not included in the first table, since they were seen during June, July, and August, three months during which we were not yet in the habit of examining every new case for this symptom. However, these 15 cases will be of use in discussing the type of child in which we find that the positive reaction occurs. The most striking feature is the large number (13) of cases of orthostatic albuminuria. Most of these, as well as the 2 cases classed as headache and the 5 classed as neurotic, the asthmatic, the case of enuresis, and cyclic vomiting, belong to the same clinical group, which has been described by Hamburger,<sup>13</sup> as children showing the "vasomotor symptom complex." These children are characterized by easily irritated vasomotor systems. Their chief complaints are nervousness, irritability, palpitation, flushing, indefinite pains for which no cause can be found, sometimes vomiting, without apparent reason, and, more rarely, fainting and pseudoanginal attacks. On examination they are usually pale, though their hemoglobin is normal; they have cold, clammy, cyanotic hands; their radial arteries, and frequently their temporals are palpable and sometimes visible, though the blood pressure is low. Their reflexes may be increased or diminished. Their urine often shows albumin, which disappears on lying down, and which usually can be increased by the assumption of a kneeling posture, as described by Jehle.

<sup>12</sup> Jahrbuch f. Kinderheilkunde, 1911, No. 6.

<sup>13</sup> Münch. med. Woch., 1911, No. 42.

The preponderance (23 out of 31 cases) of this type of child fits in well with the conclusions of Hochsinger, and emphasizes the frequency of the presence of Chvostek's sign in nervous children. In these cases this sign seems to me of much more value than the knee-jerk, and its presence in neurotic children appears to be of much more constancy than an increased patellar reflex.

Of the 31 children 6 did not show any other signs of nervousness, 5 having bronchitis and 1 mitral disease. These 6, however, were seen only once or twice. The other 25 all showed distinct neuropathic symptoms, 20 of them, as explained above, belonging to the vasomotor group.

We may conclude, therefore, that:

1. Chvostek's sign is present in 3.2 per cent. of the poor applying for treatment.

2. The sign becomes more frequent the older the child up to 19.6 per cent., at ten to fourteen years of age.

3. The presence of so great a number of positive cases here in America, where tetany is relatively an uncommon disease, is another argument in favor of considering Chvostek's sign in older children as distinct from any connection with tetany.

4. The positive Chvostek in an older child, as a rule, means a neuropathic constitution. It seems especially common in children showing vasomotor irritability, and particularly in those suffering from orthostatic albuminuria.

5. Chvostek's sign is easily elicited, and should be more often used as an adjuvant in making the diagnosis of neuropathic children.

---

## A CLINICAL NOTE ON VERRUCÆ PLANTARES.

BY RICHARD L. SUTTON, M.D.,

PROFESSOR OF DERMATOLOGY, UNIVERSITY OF KANSAS; DERMATOLOGIST TO THE BELL MEMORIAL;  
SWEDISH, GERMAN, AND WESLEY HOSPITALS, KANSAS CITY, MISSOURI.

FEW benign lesions of the skin are so troublesome to the patient or so refractory to therapeutic measures as the so-called "papilloma of the sole," or plantar wart. Although Gorju<sup>1</sup> described the condition in 1857, it was not until the publication of Dubreuilh's<sup>2</sup> classical paper, in 1895, and the careful clinical reports of Eddowes<sup>3</sup> in 1896, and of Melchior Robert,<sup>4</sup> in 1897, that a careful and accurate delineation of the symptomatology of the affection was available.

More recently, D. W. Montgomery<sup>5</sup> and Bowen<sup>6</sup> have called

<sup>1</sup> Thèse de Paris, 1857.

<sup>2</sup> Brit. Jour. Dermat., 1896, p. 195.

<sup>3</sup> Jour. Amer. Med. Assoc., July 11, 1903.

<sup>6</sup> Boston Med. and Surg. Jour., 1907, p. 781.

<sup>2</sup> Ann. de dermat. et de syph., 1895, p. 441.

<sup>4</sup> Ann. de dermat. et de syph., 1897, p. 397.

attention to the prevalence of the disorder in this country. Dr. Bailey, the medical visitor at Harvard, in a personal communication informed Bowen that the condition was quite a common one among the University students, and in boys' boarding schools. Berry<sup>7</sup> has recorded an interesting personal experience with the painful little growths. He found, upon inquiry among chiropodists, that the affection was far from unusual, although its true nature was seldom recognized, the lesion usually being regarded as a soft corn. Stelwagon<sup>8</sup> refers to the frequency with which he has encountered the lesions in dermatological practice. The condition occurs most often in active young persons, living at low altitudes. While the direct causative agent is probably microbic (Variot,<sup>9</sup> Jadassohn,<sup>10</sup> Lang<sup>11</sup> and others), certain predisposing factors can be recognized. Of these, stone bruises and similar injuries stand first, as Montgomery<sup>12</sup> has shown. Many of the patients suffer from hyperidrosis pedis. Hardaway and Allison<sup>13</sup> believe that flat foot and allied malpositions strongly favor the development of the little acanthomata.

Similar lesions occasionally are found on the palmar surfaces of the hands. I have twice seen them on the tips of the thimble fingers of seamstresses.

Superficially, a plantar wart closely resembles a large, oval callosity. The growths occur most frequently on those parts of the sole which are exposed to pressure (beneath the heads of the first and fifth metatarsal bones, and under the heel). On palpation, the lesions are painful, in some instances exceedingly so.

Histologically, the little tumors possess the essential characteristics of verrucæ vulgares located elsewhere on the body, but the long continued effects of pressure, friction, and moisture result in contour changes which are often more or less puzzling to even an experienced pathologist. Anatomically the lesions consist of a ring of stratified epidermis, which is thickest at the orificial margin, and gradually shades off to normal skin at the periphery. The central cavity, which is cone shaped, with the apex upward, is usually concealed by a thin layer of epidermis, and contains a mass of whitish, opaque, loosely interwoven tissue which is soft and resistant to the knife like wet tow (Dubreuilh). On investigation, this central projection is found to contain numerous slender papillary columns, which are extremely tender to the touch, and which bleed freely when incised.

Bowen<sup>14</sup> found that serial sections through the entire lesion showed at the border the pronounced acanthosis, papillary enlarge-

<sup>7</sup> Jour. Cut. Dis., 1904, p. 228.

<sup>8</sup> Dis. of the Skin, Philadelphia, 1910, p. 532.

<sup>9</sup> Jour. de clin. et de therap. des Infant, 1894, p. 529.

<sup>10</sup> Verhandl. d. deutsch. Dermat. Gesellsch., 1896, p. 497.

<sup>11</sup> Cor.-Bl. f. schweiz. Aerzte, 1898, p. 264.

<sup>12</sup> Jour. Amer. Med. Assoc., 1911, p. 1193.

<sup>13</sup> Jour. Cut. Dis., 1906, p. 127.

<sup>14</sup> Loc. cit.

ment, with downgrowth of the rete plugs, and marked hyperkeratosis typical of all true verrucæ. The granular layer was much thickened. There was vacuolation, with apparent, but not actual, increase in size of many of the super-basal prickly cells. This "ballooning" affected groups of cells irregularly, and without ascertainable cause, but was particularly marked toward the centre of the lesion. Usually, in connection with the vacuolation, there was a precocious development of keratohyalin, and in the centre of a well developed wart, the portion corresponding to the rete was composed of a reticulated tissue heaped up with masses and blocks of this substance. The larger portion of the tumor consisted of imperfectly keratinized horny material.

Bowen was the first to demonstrate the presence, in many of the lesions, of peculiar, small, round, highly refractile, protozoa-like, intercellular bodies which occurred in the third or fourth row of the rete, and which appeared to bear some relation to the vacuolation. These bodies stained readily by the acid reagents, and could be sharply differentiated from the rest of the nuclei. Bowen believes that they represent some form of nuclear degeneration or alteration.



FIG. 1.—Showing a typical lesion in a very frequent location.



FIG. 2.—Same lesion as shown in Fig. 1, with epidermal "lid" removed.

The two following cases of plantar warts, which have recently been under my care, are more or less typical:

CASE I.—F. B., male, student, aged nineteen years, referred to me by Dr. C. D. Trask. The cutaneous history of the family was negative. The patient had for several years been troubled with

warts on the dorsal surfaces of both hands. In September, 1910, while playing tennis, he sustained a bruise of the left heel. He paid very little attention to the injury at the time, but, six weeks later, the tenderness having persisted, he consulted Dr. Trask, fearing the periosteum was affected.

Despite curettage, and the employment of various other surgical measures, the lesion refused to heal. When I first saw the case the wart had been present for over four months, and the patient was compelled to resort to the use of a cane, in order to relieve the pressure when walking. The growth, which was located near the outer edge of the heel, was oval in outline, and measured 1.5x2.5 cm. When the epidermal "lid" was removed, by means of a sharp spoon, the hypertrophied papillæ were found to extend upward almost to the surface. The superabundant epidermis was scraped away, and the wart thoroughly frozen with carbon dioxid snow, Pusey's<sup>15</sup> method being employed. One week later this procedure was repeated, and the result was a fairly prompt and complete recovery. No anesthetic was needed.



FIG. 3.—Showing lesion in Case II after removal of superficial epidermis.

CASE II.—L. S., female, housewife, aged twenty years, referred to me by Dr. Frances Scarritt. The patient is a native of Massachusetts, and until recently resided in Lowell. Her sister-in-law, a vigorous, athletic young woman, aged nineteen years, was under my care for a similar ailment in 1909. In August, 1911, the patient noticed a corn-like thickening of the sole of her right foot, near the head of the first metatarsal bone. The lesion gradually increased in size, and became very painful. On two occasions it was treated by chiropodists, but promptly recurred, in less than a fortnight, each time.

In October, her physician referred her to a Boston surgeon, who excised the growth, under ether anesthesia. A remnant of the tumor

<sup>15</sup> Jour. Amer. Med. Assoc., 1907, p. 1354.

evidently remained, however, for, six weeks after the operation, the wart was as large, or larger, than at first.

The patient, a highly intelligent, but rather nervous young woman, was extremely sensitive to pain, and objected to even the use of the hypodermic needle. The outer layers of thickened epidermis were carefully pared away, and a 20 per cent. salicylic acid plaster prescribed, to be renewed twice daily. Later, when the cavity had become completely exposed, cocaine was applied locally, and the wart was frozen as deeply as possible. Unfortunately, the



FIG. 4.—Case II, showing a wart on toe of affected foot.

patient would not permit a very thorough application of the refrigerating agent, because of the pain, and the results were not so satisfactory as in the first case here reported. The snow was employed on three different occasions, and finally, in order to accelerate matters, the cavity was rapidly but vigorously swabbed out with pure trichloroacetic acid, followed by an alkali. No further treatment was required. At this time, seven weeks having elapsed, there is no sign of a recurrence.

The beneficial action of the snow in these cases is due to two factors, tissue destruction and post-refrigerative arterial hyperemia. Despite the argument of Fink,<sup>16</sup> who based his hypothesis mainly upon Hankin's<sup>17</sup> experimental work with soda water and with carbonic acid gas in the treatment of cholera, carbon dioxide gas has very little if any value as an antiseptic, a fact which was demonstrated by Lewis<sup>18</sup> and Porter<sup>19</sup> with not only the spirillum of cholera, but also with the bacilli of tuberculosis and syphilis.

<sup>16</sup> Brit. Med. Jour., 1910, p. 732.

<sup>17</sup> Quoted by Cranston Low in *Carbonic Acid Snow as a Therapeutic Agent in the Treatment of Diseases of the Skin*, Edinburgh, 1911, p. 147. An exhaustive and valuable monograph.

<sup>18</sup> Parkin Prize Essay, Royal Coll. of Physicians, Edinburgh, 1902.

<sup>19</sup> Ibid., 1904.

That the brief application of intense cold is of little or no germicidal value was conclusively shown by Campbell White,<sup>20</sup> in 1899. His results were confirmed by MacFayden<sup>21</sup> and MacFayden and Rowland,<sup>22</sup> in 1900.

Pusey<sup>23</sup> has suggested that an increased destructive effect can be secured by preceding the freezing by an erythema, or better, a dose of the x-rays (the resulting irritation of the vascular endothelium greatly increasing the susceptibility to obliterative endarteritis). Although the procedure was particularly recommended for use in the eradication of certain varieties of nevi, it may advantageously be employed in attacking other lesions of the skin as well, and, because of the occasionally beneficial action of the x-rays in causing the disappearance of verrucæ when used alone, is particularly applicable in the case of plantar warts.

Treatment with the snow, alone, or combined with the use of other caustics or the x-rays, is fully as effective as the older methods of excision, or destruction by electrolysis, or the actual cautery, and, particularly from the viewpoint of the patient, is much to be preferred.

## THE THERAPEUTIC APPLICATION OF P-HYDROXYPHENYLETHYLAMIN (TYRAMINE): AN ACTIVE PRINCIPLE OF ERGOT.<sup>1</sup>

BY DANIEL M. HOYT, M.D.,

FELLOW OF THE COLLEGE OF PHYSICIANS; ASSISTANT PHYSICIAN TO THE PHILADELPHIA GENERAL HOSPITAL.

ABELOUS,<sup>2</sup> in 1906, noted that a rise of blood pressure was produced from the intravenous injection of the extracts of putrid meat. In 1909 Barger and Walpole<sup>3</sup> showed that this rise of pressure was, in part at least, due to certain amine substances of which *p*-hydroxyphenylethylamin (tyramine) was the most active. A little later Barger and Dale<sup>4</sup> announced that the powerful pressor substance contained in the watery extract of ergot was mainly *p*-hydroxyphenylethylamin.

There is, further, considerable evidence to show that this amine is formed in the human intestine from tyrosin. It was found by Langestein<sup>5</sup> after prolonged peptic digestion of egg albumin. Barger

<sup>20</sup> Med. Rec., New York, 1899, p. 109.

<sup>21</sup> Lancet, 1900, p. 849.

<sup>22</sup> Lancet, 1900, p. 1130.

<sup>23</sup> Berl. klin. Woch., 1908, p. 1146.

<sup>1</sup> Read before the College of Physicians of Philadelphia, December 6, 1911.

<sup>2</sup> Soc. de Biol., May 30, 1906, i, 463.

<sup>3</sup> Jour. Physiol., March 22, 1909, xxxviii, No. 4.

<sup>4</sup> Ibid.; Proc. Physiol. Soc., May 15, 1909.

<sup>5</sup> Beit. z. chem. Physiol. u. Path., 1902, i, 507.

and Walpole<sup>6</sup> took two specimens of broth which were infected with a culture from human feces. To one tyrosin was added, and the other was used as a control. Extracts from each were tested physiologically, and it was shown that the extract from the specimen which had contained the tyrosin produced a marked rise of pressure, while the control produced a slight but distinct fall. Bain,<sup>7</sup> has added another interesting phase to this subject, though the evidence presented is far from complete, by showing that in cases of high blood pressure these pressor substances are absent from the urine, while in normal individuals they appear constantly in adult life, thus making the inference that the retention of these amines in the body is, in part at least, the cause of the high blood pressure. He attempted, also, to influence the excretion of these substances by giving the subjects medicinal doses of so-called intestinal antiseptics, and in some instances lactic acid-forming bacteria.

He states, however, that these procedures have no effect on the excretion of the pressor substances in the urine. It is to be noted that there is a distinct, though not very close, chemical relationship between these amines and epinephrin. Further, they are a constituent of two common therapeutic agents, namely, the older cod-liver oil, and, as has been intimated, the watery extracts of ergot. Gautier<sup>8</sup> isolated the base from the mother liquors obtained from the putrefaction of cod livers. The older and darker oil, therefore, contained these, because the oil used to be extracted by a process involving putrefaction. The present product does not contain them, as it is produced by a steam process and the cod livers are not allowed to putrefy. It is still insisted by many clinicians of wide experience that the older cod-liver oil possessed a more powerful stimulating action than the present purer product, and it is noteworthy that the tendency to look on this substance as simply a fat food, rather than a medicine, has gone hand in hand with the improvements in the methods of extraction. It is, however, with the amine as obtained from ergot that this paper has particularly to deal. Dale and Dixon<sup>9</sup> have outlined the physiological action of this substance experimentally.

Briefly, they have found that intravenous injection causes a marked, abrupt rise in blood pressure resembling closely that of epinephrin, save that the latent period is greater and the rise of blood pressure more prolonged, and that it is active when administered hypodermically and by the gastro-intestinal tract. Experiments on the isolated mammalian heart indicate that this rise of pressure is partly due to cardiac stimulation, while if Ringer's fluid be perfused through the isolated lung the rate of flow is not affected, indicating that there is no constriction of the pulmonary vessels. On the other hand, perfusion through a portion of the intestinal

<sup>6</sup> Loc. cit.

<sup>8</sup> Bull. Soc. Chim., 1906, iii, 35, 1195.

<sup>7</sup> Lancet, 1910, clxxviii, 1190.

<sup>9</sup> Jour. Physiol., July 23, 1909, xxxix, No. 1.



circulation and plethysmographic experiments on the ear volume indicate that there is marked constriction peripherally of those arterioles having a vasomotor nerve supply. On the uterus its influence is almost identical with that of epinephrin, producing in the cat a decrease in the muscular contraction of the virgin organ and marked increase in the contraction in pregnancy. It produces dilatation of the pupil, retraction of the nictitating membrane, widening of the palpebral fissure, protrusion of the eyeball, and secretion of tears. All these effects on the eye can be produced after the removal of the superior cervical ganglion, indicating their peripheral origin. We have then a substance that, like epinephrin, stimulates peripherally all those structures which have a sympathetic nerve supply, but is unlike it in that tyramine is more prolonged in its action, has less local effect, is less toxic, and is active when given by the mouth or hypodermically. With this summary of its physiological action it is reasonable to suppose that here we ought to have a substance that possesses the same therapeutic value as epinephrin, with the added advantages of continuous action and lessened local effect to interfere with systemic action, and a substance which is active when administered by the mouth. Of its excretion, Ewins and Laidlaw<sup>10</sup> have shown that 25 per cent. of it may be found in the urine as parahydroxyphenylacetic acid, and that the heart muscle entirely destroys the substance.

In the paper by Dale and Dixon<sup>11</sup> the first observation on human blood pressure with this substance is recorded. One of the writers took 10 mg. by mouth. His pressure before taking the drug varied between 110 and 115 mm. The pressure after taking the drug was recorded every five minutes, as follows: 124, 136, 149, 148, 135, 136, 134, 134, 122, (thirty minute interval for a meal), 130 mm. It will be seen that a rise is recorded five minutes after the taking of the drug, that fifteen minutes after the pressure has risen 34 mm., and that eighty-five minutes after there was an elevation of 15 mm. The writer repeated the above on himself, the blood pressure being taken by Dr. Lucius Tuttle, of the Physiological Department of Jefferson Medical School. Any psychical effect was here ruled out by so administering the drug that neither of us knew when the 10 mg. was taken. This was accomplished by using two glasses containing the same amount of water, into one of which the drug was placed. The contents of the glasses were taken a half hour apart, and as the substance has practically no taste in this dosage, the writer has no way of knowing when he took the drug and when the water. During the entire hour there was at no time any rise of blood pressure, but rather a distinct fall. The pressure at 7.45, before either dose was taken, was 138 mm. At 8.35 the pressure was 118, the pulse 88. This was eighteen minutes after the tyramine

<sup>10</sup> Jour. Physiol., London, 1910-1911, xli, 78-87.

<sup>11</sup> Loc. cit.

was administered. After twenty-nine minutes the pressure was 120, the pulse 82. The fall of pressure was probably due to the fact that we were working in a small office and we had several lights burning, so that the temperature of the room was constantly growing warmer during the experiment.

In a case of chronic myocarditis, 10 mg. of tyramine by the mouth, was followed in sixteen minutes by a rise of 5 mm., twenty-nine minutes after the pressure had risen 7 mm. Such a slight rise, however, can hardly be looked on as due to the drug, for a difference of 10 mm. is certainly in the range of accidental variation. One hour and thirty-five minutes later the pressure had dropped 25 mm. This was after ingestion of a large quantity of hot soup. In other words, in these two observations there is no evidence that the drug taken by the mouth in 10 mg. doses has any definite effect on the circulation. This is not in accord with the experiment of Dale and Dixon, and it is probable, therefore, that this rise of pressure was due to psychic influence, as Dr. Dale himself thinks and has said in a personal communication to that effect. Alfred Clark,<sup>12</sup> working at the suggestion of Dr. Dixon, found that the administration of tyramine by the mouth to healthy individuals produced the following results:

BLOOD PRESSURE AT TWENTY-MINUTE INTERVALS AFTER ADMINISTRATION OF  
DRUG.

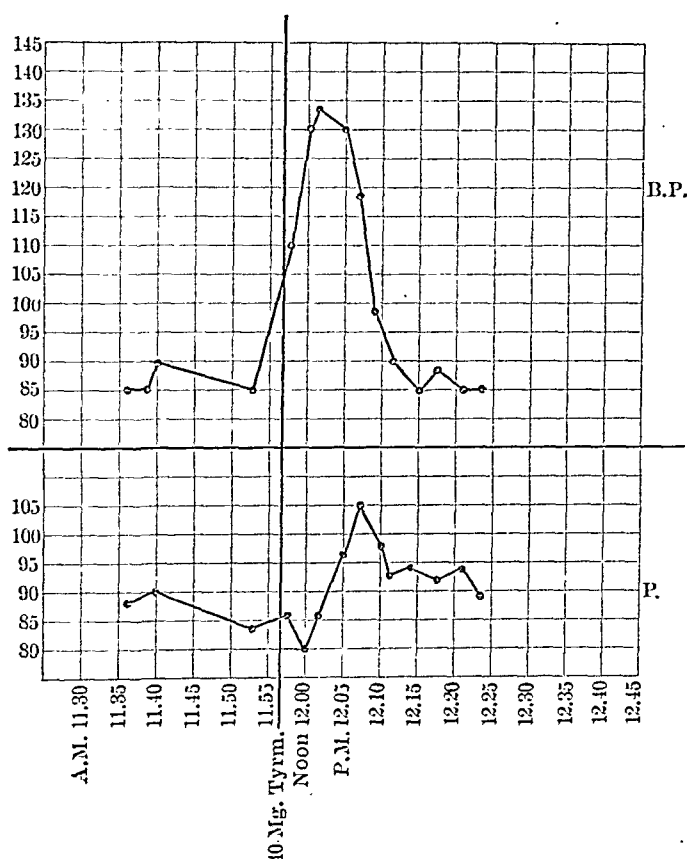
Expt.	Subject.	Dose.	0	20	40	60	80	100	120	140	160	180
I.	A. J. C.	15 mgm.	105	105	100	103	103					
II.	A. J. C.	30 mgm.	102	105	107	107	113	112		117	117	110
III.	H. D.	30 mgm.	110	118	116	116						
IV.	H. D.	50 mgm.	110	118	120	118		120	120			112

Clark also made an observation in which he gave 100 mg. by the mouth. At 10.30 A.M. the patient's blood pressure was 105, on the previous day 103. At 11.05, 100 mg. of tyramine were administered. At 11.40 the blood pressure was still 105. At 11.45, 100 mg. more were administered. At 12 noon the blood pressure was 103. At 12.30 P.M., after dinner, still 103; at 12.40, 105; 1.40, 109; 2.20, 107; 2.30, 109; 3.30, 118; 6.30, 113. The previous day at 6.30 the patient's blood pressure was 107.

It is evident from this study, with two doses of 100 mg. given at forty-minute intervals, that not until three hours and forty-five minutes after the last dose was the blood pressure distinctly raised, it being 118 mm., while on the previous day at the same time it was 105, 13 mm. higher. If the rise was due to the drug it came on very late, and was not marked.

As to the effect upon the blood pressure of repeated doses by the mouth, the writer has not yet observed a sufficient number of cases

to do more than suggest the effect. He took 3 cases of moderately advanced tuberculosis; one received 5 mg. three times a day, the other two 10 mg. each three times a day. The blood pressure records were made morning, noon, and night, taken at times by the writer, at times by Dr. Alexander, a resident physician at the Philadelphia Hospital, and by the head nurse. In two of these cases there was no evidence of any effect. In one case there was recorded a rise of pressure of 20 mm., and the day after the drug was stopped the pressure slowly fell. This one case is, as has already been said, only suggestive.



[Plotted curve showing the result of injecting 40 mg. of tyramine in toxic patient with advanced tuberculosis and marked circulatory weakness.

The effect of hypodermic injections of small doses up to 20 mg. is very slight. Clark in his paper calls attention to the fact that he found the most favorable site for systemic effect to be the loose tissue beneath the clavicle. In one case, where 10 mg. was administered, there was some evidence of action, the pressure rose 12 mm., and the strength of the heart sounds was markedly increased; the case was one of mitral insufficiency with dilatation. Only about half the systoles could be made out at the wrist. After the giving of the

drug there was a distinct improvement in the character of the heart sound, particularly as to regularity and uniformity. This effect, if any, however, was but transitory. These findings are in the main consistent with Clark's results, save as already noted he seemed to get better effect when the drug was given in the subclavicular fossa. He also obtained a greater local effect than the writer noticed. He speaks of pallor and goose-flesh at once seen around the site of the injection, followed by hyperemia. 15 mg. was followed by a rise of 6 mm. in five minutes; 20 mg. 16 mm. When, however, a dose of 30 mg. is reached the effect becomes very marked, but at the same time extremely fugacious. The accompanying chart shows a plotted curve representing the result of injecting 40 mg. subcutaneously below the clavicle in a case of chronic myocarditis with pulmonary tuberculosis, the patient being profoundly toxic.

The above distinctly illustrates several important things in regard to the action of this substance. It will be noted that four minutes after the injection the blood pressure had risen from 85 to 130, a jump of 45 mm. This patient being toxic, it is probable that the cause of the low blood pressure was in part at least vasomotor; but so sudden was the rise of blood pressure that for the time being it caused a distinct slowing of the heart, and although the drug is a decided stimulant to that organ, yet the rise of pressure was associated with a transitory irregularity. The next most striking thing is the marked fugaciousness of action. From a study of the experimental curves in the lower animals, one would expect a much more prolonged effect. In this instance nineteen minutes after the drug was given the blood pressure had again reached the normal and the cardiac rate was practically the same. In fact the picture is strikingly like that of the intravenous injection of adrenalin. Clark's results for the larger doses again correspond closely with the writer's. An injection of 40 mg. produces a rise of blood pressure of 30 mm. in ten minutes, associated with an increase of pulse rate; an injection of 50 mg. produces a rise of 50 mm., accompanied by a fall in the pulse rate; an injection of 60 mg. produces a rise of 60 mm., again with a fall of pulse rate. These were cases with practically normal blood pressure. In three cases of shock the injection of 20, 50, and 70 mm. produced approximately the same effect as in the normal cases, save that the reaction was distinctly less marked, and in no case was there any evidence of continuousness of action.

It is well understood that 20 experiments are far too few from which to draw any definite conclusion. It is to be noted, however, that the writer has selected cases in which the blood pressure was likely to remain constant, and has avoided acute shock with its natural tendency to recovery, and that, therefore, the distinct changes which follow the administration of the drug were probably due to it. Further, it will be seen that Clark and the writer, working absolutely independently, have reached practically the same con-

clusion as to the value of this substance as a circulatory stimulant. The drug is freely soluble in water, produces apparently no gastro-intestinal irritation, and when given by the mouth is uncertain and slow in its effect. When administered in doses from 20 to 40 mg. it produces a marked and abrupt rise of pressure, which is very fugacious, and is sometimes associated with slowing of the pulse rate and irregular heart action. The substance should be of value in the treatment of conditions in which there was marked vasomotor depression, but it apparently cannot be depended upon for any prolonged action.

I wish to express my thanks to Prof. W. E. Dixon and Dr. H. H. Dale for their assistance. Also to Dr. T. Mellor Tyson, Dr. William E. Hughes, Dr. L. N. Boston, and Dr. Ward Brinton for the privilege of selecting cases from their wards.

## THE OCCURRENCE OF TRICHOMONAS HOMINIS IN GASTRIC CONTENTS WITH A REPORT OF TWO CASES.

BY FRANK SMITHIES, M.D.,

GASTRO-ENTEROLOGIST TO ST. MARY'S HOSPITAL (MAYO CLINIC), ROCHESTER, MINN.; FORMER INSTRUCTOR IN INTERNAL MEDICINE AND DEMONSTRATOR OF CLINICAL MEDICINE, UNIVERSITY OF MICHIGAN, ANN ARBOR.

SINCE the active Caucasian occupation of the Philippine Islands, the West Indies, and Central America in the last decade, the study of protozoa parasitic to the gastro-intestinal tract of man has received great impetus. New and valuable facts have been brought forward by Musgrave and Clegg,<sup>1</sup> Walker,<sup>2</sup> and others concerning the biology of amebæ and flagellate protozoa, as well as the etiology and symptomatology when such are present in the human intestinal canal. Following the pioneer work of Dock,<sup>3</sup> of recent years, Freund<sup>4</sup> and Sistrunk<sup>5</sup> have shown that amebæ and flagellate protozoa, which were formerly considered to be present but rarely in the feces of individuals who had never visited tropical regions, are by no means infrequent in the discharges of persons residing in the temperate zone.

With increasing amounts of material available for proper examination, it is somewhat curious that the presence of amebæ and flagellate protozoa (particularly trichomonas hominis) outside the intestines proper has not been more frequently chronicled. A rather close scrutiny of available literature reveals the fact that

<sup>1</sup> Publications of the Government Laboratories, Manila, P. I., 1904, 93; Philippine Jour. of Sci. (Manila), 1906, I, 909; *ibid.*, 1908, iii, 77.

<sup>2</sup> Jour. Med. Research, 1907, No. 7, 379.

<sup>4</sup> Archiv. Int. Med., 1908, i, No. 1, 28.

<sup>3</sup> Texas Med. Jour., April, 1891.

<sup>5</sup> Jour. Amer. Med. Assoc., 1911, Ivii, 1507.

within the last eight years there has been but one observation detailing the presence of flagellate protozoa in the stomach, esophagus or oral cavity. In this country and abroad, it is quite likely that search for these parasites has not been made apart from intestinal discharges.

Nearly fourteen years ago Skaller<sup>6</sup> reported 2 cases of carcinoma at the cardiac end of the stomach where flagellates similar to "*trichomonas vaginalis*" (Donne,<sup>7</sup> Dock<sup>8</sup>) were discovered in the gastric extracts as well as in the patient's stools. Shortly afterward Strube<sup>9</sup> recorded a similar case, a male patient, with foul-smelling vomitus and a "hard tumor" in the epigastrium. A few years later Cohnheim<sup>10</sup> described the presence of *trichomonas hominis* in a case clinically diagnosticated "gastritis," in the test-meal extract of which the total acidity was 19 and the free hydrochloric acid was estimated at 12, and in a second case clinically "*carcinoma ventriculi*" amebæ were occasionally present. Following Cohnheim, Zabel<sup>11</sup> reported 3 cases where he had demonstrated flagellate protozoa in both gastric and intestinal contents. Two of his cases were diagnosticated "*achylia gastrica*." These had *leptothrix*, amebæ, spirillæ, and *trichomonas hominis* in the vomitus, gastric washings, and the stools. The third case was one of carcinoma of the stomach, at first with slight interference with motility, but later with marked retention and the presence of lactic acid. *Megastoma entericum* was demonstrated in the gastric extracts. Cohnheim<sup>12</sup> shortly after stated that he had seen *cercomonas hominis* and *trichomonas hominis* in cancerous involvements of the tongue and esophagus and also in the mouths of individuals with carious teeth. This observation was verified by von Leyden.<sup>13</sup> So far as we have been able to discover, the most complete study of flagellates in gastric extracts has been made by Rosenfeld.<sup>14</sup> He comments upon the fact that *trichomonas hominis* has been reported usually in extracts that show *achylia*, but claims that this does not necessarily follow inasmuch as one of his cases had a free hydrochloric estimation of 6 and a total acidity of 37. Rosenfeld describes 6 instances of the presence of *trichomonas hominis* in gastric contents, where carcinomas involved various positions in the wall of that viscus. They were frequently accompanied by long bacilli (Boas-Oppler) and *leptothrix*. The number of flagellate protozoa increased in proportion to the diminution of acidity and as retention progressed. All Rosenfeld's patients exhibited cachexia and palpable tumor in the epigastrium.

<sup>6</sup> Berl. klin. Woch., June, 1898, 551.

<sup>7</sup> Compt. rend. de l'Acad. des Sc., 1836, iii, 385.

<sup>8</sup> AMER. JOUR. MED. SCI., January, 1896, 1.

<sup>9</sup> Berl. klin. Woch., 1898, No. 32, 708.

<sup>10</sup> Deutsch. med. Woch., 1901, No. XXVII.

<sup>11</sup> Arch. f. Verdauungskrank., 1901, vii, 509.

<sup>12</sup> Deutsch. med. Woch., 1902, 174.

<sup>13</sup> Ibid., 182.

<sup>14</sup> Ibid., 1904, xxx, 1717.

We have not been able to discover a report of the finding of trichomonas hominis in gastric extracts outside of Continental literature. Perhaps a routine search for this parasite has not been made in gastric contents. Observations upon its occurrence in the stools of patients living in the northern half of the United States are rapidly becoming more numerous, as the recent study of Sistrunk<sup>15</sup> demonstrates. It would seem timely to place on record somewhat fully the following 2 cases where trichomonads were demonstrated in gastric extracts. Search for this and other parasites in gastric contents may thereby be stimulated.

## I.

### CASE REPORTS.

CASE I.—Mrs. G., aged twenty-eight years, a native of the mineral well district of Texas, was referred by Professor Aldred Scott Warthin, Ann Arbor, Michigan, August 17, 1908.

*Subjective Symptoms.* Severe headaches, coming on paroxysmally, especially following exertion, excitement, etc.; attacks of "dyspepsia," namely, nausea, belching of gas, with "sore stomach;" obstinate constipation and general weakness.

*Family History.* Negative.

*Personal History.* Was a healthy child, raised in southern Texas; married at sixteen, a widow at nineteen. Was operated upon at that time for "ovarian trouble;" made a good recovery and then commenced the study of nursing at Dallas, Texas. Later, had her appendix and one ovary removed. She overworked at the nurses' training school and had a "nervous breakdown" when aged twenty-four years. Was again married a year later, although she was not well at the time, complaining of "sore stomach," dyspepsia, and weakness. She was nauseated constantly, but never vomited. Habitual constipation resulted in hemorrhoids, which required several operations before she became comfortable. At these operations she lost much blood. The hemorrhoids bled especially freely again in the spring of 1908. Menstruation has been generally regular; patient never pregnant, never passed clots nor had leucorrhea. No urinary symptoms.

*The present trouble* dates back about two years. The main symptoms have been loss of appetite, nausea, distress after eating a hearty meal, belching of gas, severe prostrating headaches, and weakness. The headaches are most frequent and severe when the "dyspepsia" is most troublesome and when constipation is marked. The patient has lost ten pounds in weight during the last nine months. Constipation has been relieved by raw fruit

and fresh vegetable diet and large draughts of a Texas mineral well water, not boiled.

*Examination.* Temperature, 98.8; pulse, 68; respiration, 22 (3 P.M.).

Patient of medium build with moderate amount of panniculus; skin pale, sallow throughout, but not jaundiced; sclerotics and mucous surfaces pale but not jaundiced; tongue has a moderately heavy, grayish yellow, adherent coat; breath, heavy.

Mouth, nose, and throat, negative. Reflexes, negative. Thorax, negative.

Abdomen, slightly distended, navel above the level of the ribs. Slight tenderness in right iliac fossa; both kidneys easily palpable; liver and spleen negative. Rather marked gurgling throughout entire abdomen; splashing sounds on tapping between navel and pubis. On inflation, stomach holds 28 bulbs without discomfort; the lesser curvature distinctly seen at one finger's breadth above the navel in the midline, while the greater curvature is made out at four fingers' breadth below the navel in the median line.

Pelvis, right ovary and tube removed; left ovary free; uterus in good position and free; pelvic floor moderately strong; external genitalia negative (Dr. Frank Witter).

Blood: Red blood corpuscles, 4,500,000; white blood corpuscles, 6210; hemoglobin, 95 per cent. Differential formula (350 white cells counted). Small lymphocytes, 11.14 per cent.; large lymphocytes, 4.6 per cent.; transitionals, 0.57 per cent.; polymorphonuclears, 74.5 per cent.; eosinophile polymorphonuclears, 1.7 per cent.; myelocytes, 0.28 per cent.; mast cells, 0.28 per cent.; degenerates, 5.1 per cent.

Urine: Negative, chemically; no parasites seen.

GASTRIC EXAMINATION: Test meals. August 19, shredded wheat biscuit meal removed after forty-five minutes. Light yellow, gastric odor, particles well broken up; 65 c.c. recovered; lavage clear after 2 liters of water.

Chemical examination: Total acidity, 40; free Hcl., 30; Uffelmann and organic acid absent.

Microscopic examination: Numerous very active, flagellate protozoa, the majority with "ground-glass" appearing bodies; a few sluggishly moving and darker. In warm preparations, four anterior flagellæ discernible; undulating membrane seen with difficulty. The organism was recognized as trichomonas hominis and demonstrated as such to several colleagues. Many motile and non-motile bacilli. Few meat fibers well broken up; starch, erythrodextrin.

Pepsin and rennin reduced. Occult blood—negative (guaiac and old turpentine method).



August 20. Shredded wheat biscuit meal; removed sixty-seven minutes after eating; 73 c.c. recovered; lavage clear after 3 liters of water. Extract, light yellow, gastric odor; test food well broken up.

Chemical examination: Total acidity, 45; free Hcl., 20; Uffelmann, Pettinkofer's, organic acids, and occult blood absent.

Microscopic examination: Few short non-motile rods; no flagellate protozoa or amebæ seen; slight microscopic food retention.

Pepsin and rennin present but reduced.

August 21. Shredded wheat biscuit meal removed thirty-five minutes after eating; 40 c.c. recovered; light yellow, gastric odor; mucus in slight excess. Lavage and test-meal fluid, warm normal saline solution.

Chemical examination: Total acidity, 18; free Hcl, 6 (doubtless not accurate on account of normal salt being administered with test food). Uffelmann, Pettinkofer, organic acid, and occult blood absent.

Microscopic examination: Enormous number of very actively motile trichomonads seen. Many dying and dead forms, some coarsely granular and some vacuolated. In some, when the preparation was diluted with warm saline solution, undulating membranes well discernible. The trichomonads appear smaller than those seen in this patient's stool (see below) but are quite as motile. As nearly as could be estimated the average length of the body was about 12 microns. No measurements of the tails were made. Specimens were kept on the warm stage the greater part of the morning, and with the frequent addition of warm saline solution, actively motile forms were preserved. Cold, or warm, acid and alkaline solutions rapidly killed the flagellates (hydrochloric acid above 0.3 per cent.; acetic acid, nitric acid; caustic soda, caustic potash, 1 per cent. lactic acid, 0.5 per cent. salicylic acid, and 1 per cent. carbolic acid solutions were used). When the gastric extracts were diluted with aniline dye preparations (methylene blue, Gram's mixture, gentian violet, Wright's stain) in an attempt to stain the organisms, the smears showed small, contracted, scarcely recognizable dead organisms. Tubes of blood serum and glucose agar inoculated with 5 drops of gastric extract, in which actively motile trichomonads were present in large numbers, revealed not even recognizable dead organisms the following day, although there was an abundant growth of bacilli. In the gastric extract itself incubated in three volumes of normal saline solution, no trichomonads could be made out after twenty-four hours.

August 22. Fasting stomach; patient tubed at 8.25 A.M. No contents obtained. Lavage with warm normal saline solution was clear with the exception of small amounts of mucus. In the examination of seven specimens of the lavage water and bits of mucus, only one trichomonad was seen. This was found in a bit of dense mucus and was not motile, even though the preparations had been kept warm since they were secured.

August 22. Riegel dinner removed at 4.45 P.M., 160 c.c. recovered. Lavage clear after 4 liters of warm saline solution. Extract showed, macroscopically, much poorly chewed food.

Chemical examination: Total acidity, 16; free HCl, 8; Uffelmann, Pettinkofer, organic absent; occult blood, faint positive (guaiac and old turpentine method).

Microscopic examination: Several small, granular, sluggishly motile trichomonads seen; flagellæ very difficult to observe, even with subdued light. Many long slender, non-motile bacilli, usually in pairs. Food debris in various stages of digestion; mucus in excess.

EXAMINATIONS OF STOOLS. August 22. Large, greenish-brown stool following 1 ounce of domestic Carlsbad salts. Stool has peculiar foul, penetrating, musty odor. Much partly altered food and mucus, in tenacious strings and flakes. Reaction—alkaline to litmus.

Chemical examination: Skatol, positive. Occult blood, faintly positive.

Microscopic examination: Enormous numbers of large (15 to 22 microns approximately) actively motile trichomonads; no amebæ; great numbers of long slender motile and non-motile bacilli; much food debris, poorly digested; mucus in excess.

PROGRESS OF THE CASE. The following treatment was suggested: Hydrargyri chloridum mite, grains v, in divided doses at bed time, followed by 1 ounce of salts before breakfast the following morning. This medication was given twice weekly, and the stools were saved after each bowel movement. Acidum hydrochloricum dilutum was given in doses of xxx drops a half hour after meals, and repeated an hour and a half after each meal. Gastric lavage on empty stomach, with large quantities of 1 per cent. sodium salicylate solution was carried out three times weekly. Intestinal diet and boiled water were ordered.

After the patient had had two "rounds" of calomel and salts, and several lavages of salicylate of soda, trichomonads were no longer present in either gastric contents or stools. Flatulence, nausea, headaches, and weakness disappeared. The patient felt so well that in late September a trip to Canada was allowed. On October 3, she again reported saying that she felt well, although she had not been under treatment while away from Ann Arbor. A specimen of gastric contents showed no flagellate protozoa. A fresh stool examined after Carlsbad salts had been administered showed enormous numbers of motile bacilli, much mucus and many triple phosphate crystals. Examination of four fresh preparations on the warm stage revealed one large, very actively motile trichomonad.

On October 6 the patient was given 50 grains of thymol, in two doses, at bedtime, combined with 2 grains of calomel. At 7 A.M.

the following morning an ounce of Carlsbad salts was administered. The stool was foul smelling, and contained much poorly digested food, but few motile bacilli and no trichomonads were seen.

The patient went South on October 10, feeling very well. Her physician (Dr. Benj. Beeler, Mineral Wells, Texas), was advised regarding the condition present, and with his aid treatment was carried out along the above lines. The last time information was received from the patient (Spring, 1910), she was in excellent health, had gained weight, and had had no further return of protozoa in either gastric extracts or stools.

CASE II.—Mrs. J., aged forty-seven years, native of Michigan; referred by Dr. F. N. Bigelow, Holly, Michigan, April 20, 1909.

*Subjective Symptoms.* Feeling of weight high in epigastrium, immediately after eating, "sourness" of stomach, with bitter eructations, flatulence; obstinate constipation; very annoying cough; facial neuralgia; palpitation of heart; nervousness.

*Family History.* Sister died of pulmonary tuberculosis; otherwise negative.

*Personal History.* Good health until four years since. Never pregnant.

*Present Trouble.* About four years ago had stomach disturbances, which were diagnosticated "dilatation and fermentation;" suffered from chronic constipation and hemorrhoids; had a White-head operation performed for the hemorrhoids, and at that time lost a great deal of blood, with resultant weakness. After operation, stomach trouble appeared to improve. The patient *spent the last three winters in Florida.*

In the fall of 1908 had bronchopneumonia; convalesced in Florida; improved slowly; developed "whooping cough," which was so severe that vomiting frequently occurred, especially at night. Has been losing appetite, strength, and weight during the last six months. Recently developed distressing sense of weight high in the epigastrium, most marked immediately after eating, with acid eructations and regurgitation of but slightly altered food; character of food makes little difference in this respect; the eructations frequently last for two hours after meals, and are worse when lying down; vomiting relieves. Of late constipation has become very obstinate, requiring strong cathartics. When constipated, neuralgia and nervousness are aggravated.

*Examination.* Temperature, 99; respiration, 36; pulse, 92 (4 P.M.).

A moderately large, thick-set woman of asthmatic type; appreciable cyanosis of tip of nose, ears, and of lips; coughs frequently, and paroxysmally, cough having a slight "brassy" ring; sclerotics slightly injected.

Tongue heavily coated; throat—"marked enlargement, of true aneurysmal type of the ascending pharyngeal artery, from the

level of the larynx to just above the orifice of the Eustachian tube; the vessel shows marked pulsation throughout the entire field of observation" (report of Professor R. Bishop Canfield).

Neck: Marked carotid pulsation on right; no tracheal tug, or positive venous pulsation.

Thorax: Diffuse bronchitis, more marked in left lower back; moderate cardiac hypertrophy. Blood pressure: Systolic, 145; diastolic, 104 (Riva-Rocci, 12 cm. cuff.).

Abdomen: Distended and tympanitic; gurgling sounds throughout; stomach by inflation extends two fingers' breadth below the navel in the midline; tenderness high in the epigastrium and over the gall-bladder.

Radiogram: Moderate cardiac hypertrophy; great vessels negative; pulmonary edema; "dilated esophagus" (Dr. V. J. Willy).

Urine: Trace of albumin in twenty-four-hour sample (acetic and ferricyanide test).

Sputum: "Curshmann's spirals;" few alveolar cells containing blood pigment.

Blood: Red blood corpuscles, 4,560,000; white blood corpuscles, 5240; hemoglobin, 90 per cent. Differential formula—(516 white cells counted). Small lymphocytes, 9.7 per cent.; large lymphocytes, 3.1 per cent.; transitionals, 6.4 per cent.; polymorphonuclear neutrophils, 66.8 per cent.; eosinophile polymorphonuclears, 2.4 per cent.; myelocytes, 0.5 per cent.; degenerates, 10.8 per cent. No atypical red cells.

GASTRIC EXAMINATION. April 28. Test meal: Shredded wheat biscuit and distilled water; removed seventy minutes after eating. Stomach tube passed with difficulty on account of enlarged vessel in throat; patient vomited 80 c.c. of partly altered test-meal food chiefly before tube passed into stomach; 40 c.c. of a canary-yellow fluid removed through tube; the latter contained an excess of mucus, together with well-broken up food, and had a very sour odor.

"Vomitous:" Straw colored, slightly sour odor; shredded wheat biscuit poorly broken up; Congo and Gunzberg test faintly positive.

Chemical examination: Total acidity, 4; free HCl, 4; occult blood, organic acid, and Pettinkofer absent.

Microscopic examination: Poorly digested shredded wheat biscuit; one sluggishly moving, flagellate protozoon, with granular endoplasm; many motile bacilli.

Gastric Extract. Chemical examination: Total acidity, 56; free HCl, 18; Uffelmann, Pettinkofer, occult blood (guaiac and peroxide of hydrogen test) and organic acid absent.

Microscopic examination: Many rather small (average about 8 microns) granular appearing, sluggishly motile trichomonads; many globular, vacuolated, and contracted forms, apparently

dead; many leukocytes and cell nuclei; enormous numbers of actively motile, long, and slender bacilli; food particles, potato starch, shredded wheat biscuit fibers, few meat fibers well preserved, mucus in marked excess.

*Digestion.* Pepsin and rennin present but greatly diminished.

May 1. Fasting stomach; patient tubed at 9.15 A.M., 45 c.c. canary-yellow fluid removed, mixed with shaggy strips of mucus, bits of hard egg and toast; lavage with warm normal saline solution, clear after about 3 liters. Some of the first contents recovered, appeared to come from the esophagus, and were Congo negative.

Chemical examination: Total acidity, 22; free HCl, 14; Uffelmann, occult blood, and organic-acid tests negative. Pettinkofer, faintly positive. Pepsin and rennin—trace.

Microscopic examination: Few slightly motile, darkly granular trichomonads; many ovoid, balloon-shaped, and globular forms, exhibiting coarse endoplasm, frequently with large vacuoles; many short non-motile bacilli, single and in chains of from four to six; cell nuclei increased; much mucus, and microscopic food retention. This patient was not given a Riegel dinner at this time, on account of the danger of tubing due to the aneurysm of the ascending pharyngeal artery.

STOOL EXAMINATIONS. April 29. Fresh specimen secured after administration of 1 ounce of domestic Carlsbad salts on empty stomach. Large, greenish yellow, foamy, semi-fluid stool, with penetrating, acid, and musty odor; large strings of mucus, mixed with small particles of food remains.

Chemical examination: Indol and skatol, positive; occult blood, positive (gualiac and peroxide of hydrogen test).

Microscopic examination: Enormous numbers of very actively motile, generally pyriform trichomonads. The majority had finely granular bodies, and were uniformly larger than those seen in the gastric extracts of the day previous and subsequently. Some were very large, measuring from 20 to 28 microns. With subdued light, and when the protozoa were dying or entangled in mucus or food debris, four anterior flagellæ and the undulating membranes could be made out. On the warm stages, specimens were kept the greater part of a forenoon, before they became sluggishly motile, coarsely granular, contracted or large and vacuolated, preceding their death. Attempts were made to obtain stains by the carmine and the osmic acid-Wright-stain methods (as elaborated by Freund under Professor Dock's direction at the University Hospital, Ann Arbor), but with no success. The cell bodies appeared to become disintegrated in the drying and fixing, so that only poorly stained debris showed. Probably greater experience with these methods would have led to more satisfactory results. Attempts at culture in the following media were made: (1) Human blood mixed with mucus from feces which had been

previously washed in warm normal saline solution; (2) bouillon mixed with blood serum; (3) normal saline solution alone; (4) 0.5 per cent. lactic acid; 5 per cent. blood serum in normal saline solution; (5) solutions of 5 per cent. and of 10 per cent. ox bile in sodium citrate in normal saline solution; (6) ox bile alone; (7) 5 per cent. ox bile, and 5 per cent. blood serum, with 0.5 per cent. lactic acid in normal saline solution; (8) 5 per cent. ox bile, 5 per cent. blood serum in beef bouillon; (9) alkaline saliva. All methods were unsuccessful. Cold water or salt solution, or these above 110° F., rapidly caused death of the trichomonads. Solutions of organic and inorganic acids (markedly acid to litmus) and of alkalies (markedly alkaline to litmus) caused rapid disintegration of the parasites.

In the stool, in addition to the flagellates were vast numbers of actively motile bacilli. There was much poorly digested food and mucus.

May 1. Stool passed without cathartic. Medium size, in flat ribbons, soft, coated with mucus; of penetrating musty odor.

Chemical examination: Occult blood, and indol negative. Schmidt's bichloride test, bilirubin.

Microscopic examination: No trichomonads in either liquid parts of stool or in bits of mucus, although nine specimens were examined carefully; many motile bacilli; much poorly digested food.

TREATMENT. This case was treated similarly to Case I, with the exception of frequent lavages. A preliminary lavage with 1 per cent. solution of sodium salicylate was given; after that "rounds" of calomel and salts, with doses of hydrochloric acid after meals. Frequent small feedings with intestinal diet relieved the epigastric distress, the regurgitations, and the flatulence. A sedative controlled the coughing by lessening the arterial pulsations that constantly tugged at the larynx.

On June 3, the patient felt very well, had no gastric or intestinal protozoa and returned home. She was seen again, with Dr. Bigelow, in the Fall of 1910. Exposure while on a camping trip had brought on cough and some return of old symptoms in the stomach. The esophagus and gastric extracts showed no flagellate protozoa. The stools exhibited many sluggishly motile trichomonads, numerous motile bacilli, and an excess of mucus.

The patient was given a preliminary treatment of calomel and salts and when the intestinal tract was well emptied had 60 grains of thymol administered in two doses at bedtime. This was followed by a saline cathartic the following morning. The stool showed no flagellate protozoa, and few motile bacilli. The patient returned home under treatment and has not been heard of since.

## II.

Inasmuch as the above cases have been considered in detail, clinically, but little further comment appears necessary. However, it would seem proper to briefly emphasize certain facts.

Both patients were women who had resided in semi-tropical climates; both had been weakened by illness and loss of blood incident to surgical procedures; both patients had habitually partaken of unboiled water from surface wells and had doubtless also eaten freely of fresh, moist, green vegetables and fruit in all probability contaminated. Neither patient had experienced periodic or chronic diarrhea; on the contrary, obstinate constipation was present in spite of the existence of enormous numbers of flagellate protozoa and motile and non-motile bacteria in the intestinal tract. This is somewhat unusual where trichomonads are present, but the condition has also been observed by Freund<sup>16</sup> (Case VII, his series) and others. In each case, gastro-intestinal symptoms were prominent. These were nausea, flatulence, abdominal distention, colicky pains, and constipation. Skatol and indol were present in the stools and so-called "intoxication symptoms," as headaches, neuralgia, and exhaustion were observed. The blood showed slight anemia, with increase in eosinophiles and degenerated leukocytes.

The test meal revealed microscopic retention—lowered total and free hydrochloric acid (shredded wheat biscuit meal) as well as increased amount of mucus containing great numbers of bacteria and trichomonads. The stools were the characteristic greenish-brown, semi-liquid variety of protozoan infection after Carlsbad salts have been administered. Bits of mucus, occasional altered blood, rich flora, and partly digested food were concomitant with the large numbers of trichomonas hominis.

In these patients one can only surmise the source of the infection of the esophagus, stomach, and intestines by the flagellates. It may be that the finding of the protozoa in the esophagus and stomach was secondary to a primary focus in the duodenum and jejunum, the organisms passing upward through insufficient sphincter pylori. It seems probable also that the trichomonads were ingested with food and water. Some of them, protected by mucus in the lower esophagus and in the stomach may not have been immediately killed by the acid gastric secretion.

Food and water may be contaminated readily in a great many ways. Flagellates may exist in the sputum of patients with tonsillar or nasal abscess (Leuckhart<sup>17</sup>) or in sputum from non-tuberculous lung cavities, for example, bronchiectasis (Litten,<sup>18</sup> Lenhart<sup>19</sup>),

<sup>16</sup> Loc. cit.

<sup>17</sup> Die Parasiten des Menschen, 2d Aufl., Band I, p. 315.

<sup>18</sup> Beit. z. Zentralbl. f. klin. Med., 1886, No. 5, 69.

<sup>19</sup> Microscopie und Chemie am Krankenbette, p. 61 (Dock).

or where individuals are affected with markedly carious teeth (v. Leyden,<sup>20</sup> Prowazek,<sup>21</sup> Theobald<sup>22</sup>), or oral cancer (Cohnheim). Dock<sup>23</sup> has mentioned the finding of trichomonads in the discharges of snails, frogs, and ducks. The stools of patients affected with typhoid fever, amebic dysentery, cholera or enteritis, primary or secondary to malignant disease of the stomach or bowel, may be rich in trichomonads (Dock,<sup>24</sup> v. Jaksch,<sup>25</sup> Epstein,<sup>26</sup> Davaine,<sup>27</sup> Grassi,<sup>28</sup> May,<sup>29</sup> et al.). Hunt<sup>30</sup> has reported the finding of flagellates in perineal abscess, Cunningham<sup>31</sup> noted their presence in a case of abscess of the liver. As Dock<sup>32</sup> has observed, the presence of trichomonads in urine may be responsible for wide dissemination. The possibility of resistant spore forms of the flagellates explains their viability under adverse conditions.

Morphologically, the parasite seen in the 2 cases here reported differs very little from the classic picture of trichomonas hominis as established by Donne<sup>33</sup> and Dock.<sup>34</sup> Inasmuch as the protozoa described by these and other observers and ourselves showed four anterior flagellæ together with an undulating membrane, it would seem that the "new" form of trichomonas recently described by Alexieff<sup>35</sup> conforms only to type. It might be observed that the trichomonads seen in the gastric extracts in our cases were approximately but half so large as those found in the stools of the same host. They seemed less resistant to external influences, but in other respects resembled the larger variety.

The cases presented contribute no facts regarding the much debated question of trichomonas hominis as an etiological factor. Certainly its removal in quantity from the gastro-intestinal tract of its host is attended by clinical benefit. It has been advanced frequently that the presence of great numbers of flagellates acts as a mechanical irritant to the intestinal mucosa or that such protozoa secrete a substance which is irritant. While these observations may be true, we feel that other factors might be considered.

The rapid multiplication of intestinal bacteria and protozoa (as trichomonads) results in a great quantity of protein-containing flora in all stages of viability. In the life cycle of the trichomonas dead forms necessarily result. What action succus entericus or associated bacteria and the like have toward hastening this death we are not prepared to state. The dead forms impose upon the digestive juices an excess of protein ("foreign proteid") for cleavage

<sup>20</sup> Loc. cit.

<sup>22</sup> Centralbl. f. Bakteriologie, 1904, p. 86.

<sup>24</sup> Loc. cit.

<sup>26</sup> Präger med. Woch., 1893, No. 38, 40.

<sup>28</sup> Compt. rend. de la Société de Biologie (Paris), 1854, i, 129.

<sup>30</sup> Zeitschr. f. klin. Med. (Berlin), 1897, xxxi, 442 (Janowski).

<sup>32</sup> Arch. f. klin. Med., 1892, Band xlix, 51.

<sup>34</sup> Quart. Jour. Mic. Sci., 1881, xxi, 234.

<sup>36</sup> Loc. cit.

<sup>38</sup> Compt. rend. Soc. de Biologie (Paris), 1909, lxxvii, 712.

<sup>21</sup> Arch. f. Parasitenkunde, 1902, p. 166.

<sup>23</sup> Loc. cit.

<sup>25</sup> Wien. klin. Woch., 1888, xxv, 511.

<sup>27</sup> Lancet, London, July, 1906, 28.

<sup>29</sup> Loc. cit.

<sup>31</sup> Loc. cit.



As the work of Vaughan<sup>36</sup> and his associates has shown, this protozoic protein can be considered homologous to any other protein, chemically. The hydrolization (cleavage) of this protein by digestive ferments or associated bacterial enzymes, results in the production of so-called "toxic" and "non-toxic" groups. These may be further split to amino acids or simpler radicles. It is suggested, in view of these facts, that these cleavage products of the protein contained in the flagellates may be a not inconsiderable influence either as (1) a gastro-intestinal irritant; (2) a factor in altering metabolic change in digestive glands; (3) a source of so-called "intoxication symptoms" clinically.

---

## SACRO-ILIAC DISPLACEMENT.

BY JAMES K. YOUNG, M.D.,

ASSOCIATE PROFESSOR OF ORTHOPEDIC SURGERY, UNIVERSITY OF PENNSYLVANIA; PROFESSOR OF ORTHOPEDIC SURGERY, PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF ORTHOPEDIC SURGERY, WOMAN'S MEDICAL COLLEGE, PHILADELPHIA.

IN order to facilitate a study of sacro-iliac displacements, and to arrive at a clearer understanding of the parts involved, it becomes necessary to review the anatomical peculiarities of that articulation, as well as the mechanism of the pelvis, with its correlated structures, in so far as they relate to the subject about to be discussed.

**ANATOMY.** The sacro-iliac articulation partakes both of the nature of a true and a half joint. It possesses a hyaline articular cartilage, a synovial membrane, and a capsule, and it derives its strength and toughness from its anatomical position as well as from its powerful ligamentous attachments.

This pelvic joint which is formed by the opposed cartilage-covered surfaces of the sacrum and ilium, separated by a synovial cavity enclosed in the sacro-iliac ligament, is well fortified by many layers of strong ligamentous fibers, that not only fill the interval between the two contiguous bones, but are firmly attached to the rough iliac area behind its articular surface and which extend to the back of the lateral masses of the sacrum.

This posterior sacro-iliac ligament is far more important than the oblique sacro-iliac, which passes from the posterior superior iliac spine to the second and third sacral vertebræ. The ilio-lumbar ligament, a triangular band of strong fibers, and the sacro-lumbar ligament, a bundle of diverging fibers, likewise contribute

<sup>36</sup> Vaughan, Cumming, and Wright, *Zeitschr. f. im. und exp. Therapie*, Band ix, Heft 4, 1911, May 13.

to the stability of the joint. At times before the approach of senility this articulation may be found in an ankylosed state.

The irregular shape of the pelvis will at once invite attention. In the fetus its outline is decidedly funnel-like, while the subsequent development of its peculiarities and irregularities, including the flaring surfaces of the ilia and the normal sacral curve, are ascribed to the weight of the body, the counterpressure of the femora, and the force exerted by the ligaments. The interruption in the bony contour of the pelvis at the pubic symphysis and at the sacro-iliac articulations adds materially to the strength of the structure, and at the same time lessens the effects of shock.

It seems worthy of note that the articulation at the symphysis pubis is amphiarthroidal in character and as known to every obstetrician is capable of an "up-and-down" movement, and also of a separation of the pubic bones with a corresponding movement in the sacro-iliac articulation of the same side. The symphysis plays a dominant role in the study of obstetric mechanics. In the operation of symphysiotomy, the motion which permits of the separation occurs in the sacro-iliac joints, the pubic bones move downward and outward, contributing largely to the pelvic space gained, at the same time the sacrum, moving upon a horizontal axis, so adjusts itself by its inherent rocking motion as to widen the birth canal. It is a well-known fact to all obstetricians that in Walcher's position (in which the patient is placed in the supine position, with the hips in extreme elevation at the edge of the bed or table and the thighs hanging in extreme extension) the superior strait is enlarged by a displacement of the sacro-iliac articulation. In this position it has been estimated that the conjugate or sacropubic diameter is increased 5 to 13 mm. ( $\frac{1}{5}$  to  $\frac{1}{2}$  inch approximately).

Recently the sacro-iliac articulation has been made the subject of exacting inquiry, and through their investigations clinicians and anatomists offer the statements that this articulation is a true joint that permits normally of some motion. The truth of this assertion has been demonstrated in many instances, for it has been found that when the integrity of the ligamentous attachments binding the various parts of the pelvis or of the pelvis and the contiguous bony structures has preserved its normal tone, a certain degree of movement at the sacro-iliac articulation is compatible with perfect health. Likewise, it is evident that whatever tends to disturb this balance in the economy or in any way interferes with the associated musculature, later to be mentioned, will of necessity disarrange the harmonious action normally maintained, and result in an increased movement in the articulation under discussion.

It is at least convenient to refer to the sacrum as the "keystone" of the pelvic arch, notwithstanding the criticism of accurate students

that its anterior is broader than its posterior surface. Suspended between the ilia, broader in the female than in the male, with its articular surface including half its lateral aspects, this bone is important, not only for its muscular and ligamentous attachments, but also for its resulting rocking movements upon a horizontal axis, situated at or about the middle of the sacro-iliac articulation. The sacrum is steadily anchored in place by the anterior and posterior sacro-iliac ligaments, which bind it to the ilia, while its lower portion is maintained by the sacrosciatic ligaments.

We need say but a few words about the axial skeleton to understand, in brief, the action of the musculature previously referred to, and to give a passing thought to the superincumbent body weight which normally poises itself in perfect equilibrium.

The flexuous spinal column gracefully describes the three upper curves between the occiput and the sacrum. That portion of the spine which articulates with the ribs allows of muscular attachments. Throughout this important region are found the deep muscles of the back, exerting powerful actions from the coccyx to the occiput. Their concerted action extends to the spine, while their contraction on one side only produces a lateral bending of the spine.

Passing from the pelvis to the lower limbs are the iliacus and the psoas muscles, which exert their action in a direction opposite to those of the deep muscles of the back. The psoas takes origin by five slips, the first of which starts from the contiguous borders of the last thoracic and first lumbar vertebra, the last takes its attachment from the corresponding borders of the two lower lumbar vertebræ. The fan-shaped iliacus muscle arises from the inner surface of the iliac crest, from the iliac fossa, and by a few fasciculi from the iliolumbar ligament and the contiguous portion of the ala of the sacrum. The fleshy fasciculi descend and converge to terminate with the tendon of its companion muscle, the psoas, into the lesser trochanter of the femur. From this brief description it is evident that the iliopsoas muscle is a powerful flexor of the hip-joint, or it bends the lower limb on the body or the body on the thigh.

This antagonism in action to the deep muscles of the back is essential to the correct equipoise of the body, and it finds expression in the normal ligamentous attachments supporting the pelvic girdle; for if the integrity of the articulation be interfered with, or the restraining muscular adjustment be disturbed, the normal relationship existing between the trunk and the lower extremities must of necessity be broken. To qualify this last statement, it should be remarked that the superimposed body weight does not displace the sacrum, because of the sinuous outline of the contiguous iliac and sacral surfaces, and by the normally resisting action of the sacro-iliac and sacrosciatic ligaments.

**ETIOLOGY.** Some of the more common effections have their origin in an abnormal sacro-iliac articulation or in the nervous structures in close proximity to it. Not infrequently an obscure case of sciatica, lumbago, backache, or kindred affection finds its etiology in a too movable sacro-iliac articulation, while any impoverishment of bodily health following the inroads of prolonged illnesses may likewise weaken this articulation. The same statement holds true in cases of direct trauma or where the joint is made to suffer from the effects of muscular strain.

The normal tonicity of the pelvic ligaments suffers a disturbance in many instances of passive congestion, hence some of the rather usual symptoms in pregnancy and menstruation.

The intimate relation existing between the sacro-iliac articulation and the sacral plexus and the lumbosacral cord would seem at times to explain the causative factor of nerve pains and nerve irritations, referable to branches and terminal filaments of these nerves. A too relaxed condition of the sacro-iliac ligaments would in itself be sufficient cause for severe neurotic paroxysms, or the pain produced may be directly traceable to the pressure exerted by pathological processes the result of inflammatory exudates.

**PATHOLOGY.** From previously adduced statements it has been shown that the sacro-iliac articulation possesses tenacity and strength, and that the joint is normally capable of some movement.

Conversely, anything that disturbs the normal tonicity of the pelvic ligaments or disarranges the reciprocal relationship between the opposing groups of muscles, previously referred to, will of necessity engender some pathological state, either in the articulation itself or in a part contiguous to it.

The simplest type of sacro-iliac affections is strain, which is usually corrected when the necessary groups of muscles so adjust themselves as to afford a rapid disappearance of the symptoms. But if the position of the strain be continued, there results a displacement or giving way of the ligamentous attachments, associated with marked instability in the joint, dependent largely upon the amount and character of the bony displacement.

The sharp sudden pain, commonly designated a "stitch" in the back, finds its pathological counterpart in the sacro-iliac joint. The lancinating pain is concomitant with a rupture of some fibers of the sacro-iliac ligaments, which allows of an abnormal degree of movement, with partial luxation of the joint. In the more pronounced cases there is evidenced a complete dislocation, where voluntary replacement may become impossible.

But even in cases of slight luxation of the sacro-iliac articulation the other joint structures in the pelvic girdle are prone to suffer, and hence, the disability to raise the body from the recumbent posture. Again, the intractable nerve pains, so frequently referred to the leg and thigh, and variously designated as neuralgia or

sciatica, with areas of anesthesia and hyperesthesia, find their origin in some pathological condition of the sacro-iliac joint, which condition is reflected along the course and distribution of the sacral plexus or lumbosacral cord.

Bilateral lesions of this articulation are not infrequently diagnosed; the result of a depraved state of health following in the wake of prolonged illnesses. As a consequence, there is found an instability of the pelvic joints, with an abnormal degree of movement at the sacrum and the development of the so-called "flat back." The weakened and relaxed sacro-iliac ligaments are thus rendered extremely vulnerable to the inroads of pathological processes, which leave them in a weakened and debilitated condition.

No matter if the joint disturbance be produced by obstetric or gynecological causes resulting in pelvic relaxation, or if traumatic, neurotic, or other influences contribute to an impairment of the articulation, it must always be remembered that ligamentous changes and perhaps their disorganization too frequently invite disaster by offering a fertile field for the invasion and development of infecting processes, not the least conspicuous of which is tuberculous arthritis.

**CLINICAL VARIETIES.** In order to systematize the study of sacro-iliac affections, it is both logical and convenient to group these cases into different classes in so far as they present the same general clinical manifestations. The two important types that need claim attention are the traumatic and the static.

*Traumatic.* The former class of cases is frequently encountered, the exciting cause either being direct trauma or indirectly the result of muscular action. The damage inflicted upon the joint structure is not commensurate with the severity of the exciting cause. The latter may be very slight, as may be instanced, in a person making a quick step from a moving vehicle where the injury to the joint may be quite as severe, as in the case of the laborer who exerts all his physical power in lifting a load, the entire force of his efforts being thrown upon the sacro-iliac articulation, with a luxation or partial luxation of the bony surfaces of the ilia and the sacrum. The lesions in the traumatic type are usually unilateral, but they also may be bilateral. Even the act of sitting down precipitately, a sudden slip or stumble or fall may be a sufficient exciting factor to produce a condition in the articulation varying anywhere from an ordinary strain to a laceration of the ligamentous union. Football, baseball, horseback riding, and other amusements furnish the proper elements for the production of this lesion. Bilateral displacement is exceedingly rare. Walking in a squatting position with a heavy weight in the hands was responsible for its production in one of the author's cases. Recurrence of these symptoms is frequently seen.

The bedridden sufferer and the patient confined to bed in prolonged illnesses frequently develop a persistent and rebellious form of backache, while sacro-iliac strain is commonly found in patients coming from the operating table, where the lumbar spine has suffered an effacement from the long period consumed in the administration of the anesthetic.

Traumatic sacro-iliac strain may also result from a shortened limb, from deformities of the hip, or from those conditions that throw the burden of the body weight almost wholly upon the sacro-iliac articulation, as is evidenced in pronounced cases of Pott's disease, and in cases of extreme lordosis, where the sacro-iliac joints suffer at the expense of the normal spinal movements, resulting in a forward tilting of the sacrum. In this connection mention must be made of diseases impairing the integrity of the lumbar and pelvic joints. Thus in spinal osteo-arthritis the cartilaginous changes and the general enfeeblement of the ligaments make this articulation the frequent and constant seat of strain, due in many instances to trivial causes.

*Static.* The so-called static variety of sacro-iliac affections is essentially mechanical in character, although it is frequently impossible accurately to determine if it is the orthopedic condition primarily or the presence of an intrapelvic process that may act as the predisposing factor in the joint disturbance producing static backache. The static variety is most largely comprised by the neurotic and the uterine.

The former class of cases is frequent in those of a highly nervous organization where the nerves and muscles are kept through unremitting excitement in a constant state of tension. These individuals are only afforded muscular relaxation during sleep, and this intermittent relaxation, together with the anesthetic and hyperesthetic area so commonly found in the lumbar and sacral regions, is often associated with impairment of bodily strength, so that this class of patients not infrequently suffer from obscure nerve pains referred to as neuritis, backache, and sciatica, which really have their origin in a sacro-iliac strain. In many of these individuals the muscles of the back may be found in a state of spasm, or the pelvis may be tilted, giving rise to an apparently shortened limb. These spasmodic muscular contractions, unlike those of the traumatic variety, extend high up into the occiput, and while the flat back characteristic of the traumatic type may be found, it is more usual to encounter a condition of lordosis with an anterior tilting of the pelvis.

The uterine variety of the static type finds expression in manifold intrapelvic conditions varying anywhere from the discomforts often attending menstruation, to the presence of tumors, the after-effects of childbirth, etc. Relaxation of the ligaments of the pelvic girdle in these conditions gives rise to abnormalities in the sacro-

iliac joints. In the more severe class of cases, actual displacement of the joint may occur, simulating the symptomatology of the traumatic variety, in that the patient almost fears to walk or move because of the necessary restriction of spinal movements, and from the agonizing nervous paroxysms experienced in the lower limbs. In menstrual disorders the relaxation of the pelvic ligaments causes intermittent symptoms, principally noted at the menstrual epoch, but where the etiological factor is intrapelvic disease, the symptom complex is permanent. It has been asserted that intrapelvic conditions may cause sacro-iliac disease or be caused by it.

**SYMPTOMATOLOGY.** The symptoms most characteristic of sacro-iliac affections are: (1) Pain; (2) limitation of motion; (3) abnormal mobility; (4) changes in attitude.

*Pain* is a characteristic symptom. It is usually referred to the sacro-iliac joint, to the sacrum, or to those areas of the lower limbs traversed by the nerve trunks or branches, that near their origin are found in close proximity to the sacro-iliac joint, namely, the sacral plexus and the lumbosacral cord. These pains are of two varieties: Those due to joint strain and those due to direct joint pressure. In the first of these varieties the pain experienced is usually greater in one or the other leg, although both legs may suffer equal degrees of intensity of pain. These pains, which are aggravated at night, find their causation in the strain placed upon the pelvic joints, although much suffering may be experienced during the day should the pelvic joints be used and strained, as is illustrated in cases where much stair climbing is required, etc.

In the second variety the pain is produced by direct nerve pressure, caused by the displacement of the articulation. The sharp, roughened edge of the articulation is thrown directly against the nerve trunk, and the pain is referred along the course of the sciatic nerve and throughout its peripheral distribution. It is to be remarked that swelling, which is a classical sign in infectious processes involving this joint, is absent in strain.

*Limitation of Motion.* This may be observed in the motion of the body upon the thighs, or *vice versa*. Again, the downward displacement of the ilium, which produces elongation of the limb and shortening of the hamstring tendons, limits the range of extension and affords a characteristic test. In the standing posture, lateral bending is more limited than normally, but not to so marked a degree as is forward bending. In lateral bending the limitation of movement is inclined away from the seat of the lesion (Fig. 1).

For clinical purposes, Kernig's test is one of the most used and one of the most reliable means in arriving at a diagnosis. The limbs are tested one at a time. The patient is placed upon his back and the unaffected limb is raised, with the knee fixed, and the degree of flexion of the hip-joint is noted. The affected

knee is then tested in a similar manner, when it will be observed that flexion at the hip-joint offers a much more limited degree of motion, due to the contraction of the hamstring muscles and the pain occasioned along the course of the sciatic nerve.

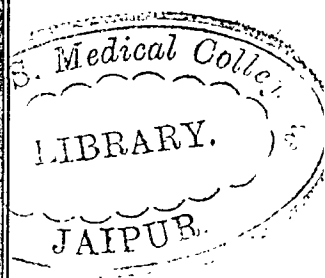


FIG. 1.—Characteristic attitude: severe unilateral sacro-iliac displacement.

*Abnormal Mobility.* Relaxation of the sacro-iliac joints from long-continued strain will greatly augment passive motion in these joints. Probably the best method for testing abnormal mobility is to ask the patient to stand with the knee fixed, and have him raise and lower the heel from the ground in rapid succession. By this test I examined a patient in the dispensary service of the



hospital of the University of Pennsylvania, and was able to demonstrate a sacro-iliac mobility of  $\frac{3}{4}$  inch.

*Changes in attitude* are incurred by alterations in the joint. Spasms of the hamstring muscles interfere with the forward movement of the thigh and thus impede locomotion, the patient assuming a stooping posture, or he bends forward. In the erect position the trunk is thrown in a direction opposite to the lesion, while the shoulder on the affected side is lowered. In stooping, flexion of the trunk is intuitively avoided, and the patient accomplishes the act by flexing the knees, similar to the attitude assumed by sufferers from spinal diseases, where the spine is held rigid.

**TREATMENT.** The treatment of sacro-iliac affection includes (1) reduction; (2) the employment of apparatus, and (3) the after treatment.

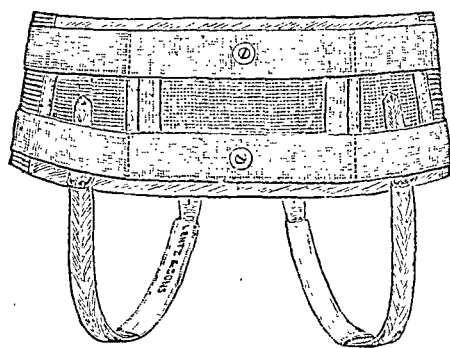


FIG. 2.—Author's brace for sacro-iliac displacement, posterior view.

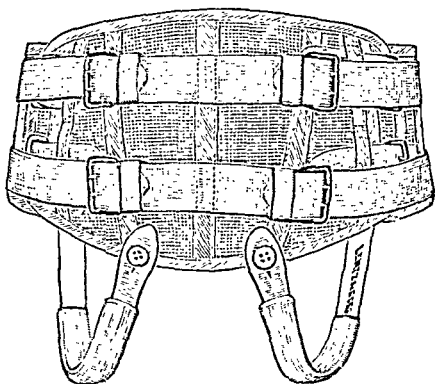


FIG. 3.—Author's brace, anterior view.

1. *Reduction* may occur spontaneously, the contiguous bony surfaces assuming their normal relations, although recurrences are likely to take place from time to time. When the reduction cannot be effected in the above manner the result can be best accomplished by placing the patient upon the face and producing forced extension, with traction of the limb. Or the patient may be placed between two chairs, situated at an interval of about a foot and a half, the surgeon making downward pressure over the site of the articulation.

2. *The Employment of Apparatus.* The simplest form of apparatus is a broad belt made up of a surcingle with two buckles. Such a belt is frequently worn by workmen from choice as a preventive measure against future displacements. A useful device that has won much favor is the spider-like brace of Osgood. It consists of a heart-shaped pad, two uprights and four lateral steel bands, which are so incorporated that the corset thus formed exerts pressure upon the sacrum.

A most efficient apparatus is that devised by the author (Fig. 2), and consists of a combination of an abdominal supporter of

special construction and a well-cushioned, triangular pad, so as to exert required pressure upon the sacrum. Pressure on the upper or lower portion of the sacrum is regulated by means of two hard-tempered semicircular springs, to which webbing straps firmly attached are buckled in front. The pressure may be centred upon the upper region of the sacrum by drawing the upper straps tight while the lower ones are allowed to remain moderately loose, and *vice versa*; pressure may be made upon the lower region of the sacrum by drawing the lower straps tight. When required the apparatus may be retained in position by perineal straps, but when it is well fitted these are not necessary.

The principle sought for in any or all such appliances is the exertion of pressure upon the sacrum, either at its upper or lower part, according to the indications in the individual case.

Where deformity has existed for a long time it may become necessary to apply traction while the patient is in bed for a varying period before employing these appliances, while in some cases it is essential to fix the trunk and lower extremity until the subsidence of the active inflammatory symptoms.

3. *The after treatment*, which is often neglected, consists in developing the affected region by means of exercises, massage, vibration, and the application of the electric current to all the ligaments and fibrous structures around the articulation, so as to prevent future displacements. These *séances* should be prolonged and should be administered over long periods of time, in order to obtain the best possible effects from this line of treatment. Should any disease of the female genital organs be associated with displacements of the sacrum it is unnecessary to remark that the former class of affections should at once engage the attention of the gynecologist. In certain cases where non-operative measures have failed to give encouraging results, I contemplate some radical surgical operations, as plating the pubic bones and wiring the sacro-iliac articulation.

---

## HEMOLYSIS IN VIVO AND IN VITRO AS DIAGNOSTIC OF CANCER.

By L. W. GORHAM, M.D.,

AND

HANS LISSER, M.D.,

BALTIMORE.

(From the Research Laboratory, Phipps Tuberculosis Dispensary, and the wards of the Johns Hopkins Hospital.)

THIS work was undertaken for the purpose of comparing the skin reaction for carcinoma described by Elsberg, Neuhof, and

Geist,<sup>1</sup> with the hemolytic power *in vitro* of the serum of cancer patients, and to study the relation, if any, existing between these phenomena and the normal isohemolysins and isoagglutinins.

A number of observers have sought for some specific or diagnostic character of the serum of cancer patients. With this idea in mind, Crile<sup>2</sup> reported having found a marked hemolyzing power on the part of the serum of cancer patients, when allowed to act upon red blood cells of a normal individual. This he found in a surprisingly large number of early cases, although he stated that the reaction disappeared when the disease became advanced. Crile's work has not been generally confirmed. Other investigators have found cancer sera to possess hemolyzing power, but in a far smaller percentage of cases than Crile did. No one has been able to prove definitely the presence of a specific diagnostic substance in cancer serum. As to specific hemolysis, further study has shown the existence of isohemolysins in normal individuals and in a variety of diseased conditions. The hemolytic test of a serum *in vitro*, therefore, is considered of no great value from the clinical standpoint. Krida<sup>3</sup> has collected from the literature a total of 1812 observations by ten different workers on the hemolysins of cancer serum tested *in vitro*. Four hundred and seventy-two cases were carcinoma. Of these, 317 (67 per cent.) gave positive hemolytic tests, and 79 were benign tumors, of which 1 (1.25 per cent.) was positive. Five hundred and seven observations were made in a variety of diseases of which 74 (15 per cent.) gave a positive reaction. Five hundred and nine observations were made on normal individuals, of which 14 (2.6 per cent.) were positive.

Both the work of Moss<sup>4</sup> and our own investigations emphasize the inconstancy of the occurrence of hemolytic properties in the serum of carcinomatous patients when tested outside the body. They demonstrate, further, the not infrequent hemolytic power in the serum of normal individuals, and as well, in the serum of patients suffering from diseases other than cancer.

Weil<sup>5</sup> has studied the hemolytic action of extracts of normal organ and of tumor on normal red blood cells. He finds that extracts of necrotic tumors and of autolized organs possess much more hemolytic power than extracts of normal organs and of non-necrotic tumors. The hemolysin in the former is dialyzable and not inhibited by the action of serum, while that of the latter is non-dialyzable and serum inhibits its action. On this basis he seeks to explain the anemia and cachexia of malignant disease, suggesting

<sup>1</sup> AMER. JOUR. MED. SCI., February, 1910.

<sup>2</sup> Jour. Amer. Med. Assoc., June, 1908, No. 23, 1, 1883; Ibid., December, 1908, No. 24, 11, 2036.

<sup>3</sup> Albany Med. Ann., No. 5, xxxi, 259.

<sup>4</sup> Johns Hopkins Bulletin, March, 1910, xxi, No. 228.

<sup>5</sup> Jour. Med. Research, 1907, p. 287; Ibid., 1908, xix, 281; Jour. Amer. Med. Assoc., 1908, li, 158; Jour. Med. Research, 1910, xxiii, 85.

that it is due to the destructive action on the red blood cells of substances liberated by the necrotic tumors.

The resistance of the red blood corpuscles to varying percentages of hypotonic salt solution has been studied in many conditions. It has been shown that in secondary anemias there is an increased resistance of the red cells.

The idea of testing the resistance of normal red cells in cases of carcinoma, by subcutaneous injection of the washed cells was suggested by Elsberg, Neuhof, and Geist.<sup>6</sup>

Krida<sup>7</sup> repeated the work of Elsberg, Neuhof, and Geist, and reported a series of 76 tests. Of 12 cases of carcinoma the reaction was positive in 9 (75 per cent.). He does not separate the cases into early and advanced carcinoma, as do Elsberg, Neuhof, and Geist. He justly raises the question as to whether this line is to be drawn. He did not find the reaction consistently absent in miliary carcinoma, as did the above observers. Krida states that if all their cancer cases are considered together, making 80 in all, the percentage of positive results would be about 77 per cent., a figure approximately identical with his own.

Risley<sup>8</sup> has also repeated the test in 100 cases at the Massachusetts General Hospital. The reaction was positive in 9 cases (33 $\frac{1}{3}$  per cent.) of malignant disease, negative in 16 cases (59 $\frac{1}{3}$  per cent.), and questionable in 2 cases (8 $\frac{1}{3}$  per cent.). In non-malignant cases of various kinds, 15 (20 per cent.) gave a positive reaction, 55 (75 per cent.) gave a negative reaction, and 3 (15 per cent.) gave a doubtful reaction. He concludes that the test is only suggestive, and thinks it is rendered practically valueless as a diagnostic aid, because of the fact that there are undoubtedly present in the blood of many patients other lysins of unknown nature, which bring about hemolysis of varying degree.

The technique employed by Elsberg, Neuhof, and Geist consisted in the subcutaneous injection into the forearm of 5 minims of a 20 per cent. suspension (in normal salt solution) of washed human red corpuscles. These corpuscles were obtained from a normal healthy individual. They state that the reaction begins to appear as a rule, about five hours after the injection, gradually increasing in intensity until it has reached its height in six to eight hours. When fully developed the reaction appears as a somewhat irregular oval area measuring from 1 x 2 to 3 x 5 cm., with a well-defined margin. The margin is often surrounded by a whitish areola. The color varies from a brownish red to a maroon, with, rarely, a bluish tinge. The lesion is distinctly raised from the surrounding skin, slightly boggy on palpation, and often somewhat tender between the time of appearance of the reaction and its fading vary. When the lesion has disappeared there remains behind a flat yellowish or

<sup>6</sup> Loc. cit.

<sup>7</sup> Loc. cit.

<sup>8</sup> Boston Med. and Surg. Jour., No. 4, clxv, 127.

greenish discoloration, such as is left by any ecchymosis. Negative cases show either the point of needle puncture only or a small flat area of varying color; rarely the skin is raised but of normal color. Their work comprised 684 injections in 432 patients, and, in brief, an analysis of their cases showed a characteristic, easily recognizable reaction at the site of injection in 89.9 per cent. of cases suffering from carcinoma, and no reaction in 94.3 per cent. of cases from carcinoma.

At first we followed their technique, giving 21 injections to 21 patients; 15 of these patients, suffering from various medical diseases other than cancer, gave negative reactions.

One white patient of this series of 21, who had an adenocarcinoma of the rectum, showed a marked positive reaction.

One case of acute endocarditis with purpura, as one might expect, showed a strongly positive reaction.

The remaining 4 cases were colored patients, of whom 3 were cancerous. No reaction could be recognized in them, because of the pigmented skin. Negroes were not used in later observations.

One case with anacidity, on whom exploratory laparotomy was advised because of the suspicion of cancer of the stomach, gave a negative reaction. Subsequent operation disclosed gallstones and no carcinoma.

NORMAL ISOAGGLUTININS AND ISOHEMOLYSINS. At this juncture the communication of Moss,<sup>9</sup> "Studies on Isoagglutinins and Isohemolysins," suggested the possibility of a relation between the skin reaction described by Elsberg, Neuhof, and Geist, and the presence of normal isohemolysins. Were such the case, the value of the test from a specific diagnostic standpoint would be *nil*.

It seemed to us that the only confirmation of the skin reaction that was to have a real scientific value must include a determination of the grouping of the patients and an injection into each patient of red blood cells belonging to each of the four agglutinin groups. Thus a ready comparison could be made between the reaction *in vivo* and that in the test-tube.

Moss is of the opinion that every human being will fall into one of the following four groups, and that this grouping is established shortly after birth, and does not vary through life, in health, or in disease.

- |           |   |   |
|-----------|---|---|
| Group I   | { | Serum agglutinates no corpuscles.                       |
|           | { | Corpuscles agglutinated by serum of Groups II, III, IV. |
| Group II  | { | Serum agglutinates corpuscles of Groups I and III.      |
|           | { | Corpuscles agglutinated by serum of Groups III and IV.  |
| Group III | { | Serum agglutinates corpuscles of Groups I and II.       |
|           | { | Corpuscles agglutinated by serum of Groups II and IV.   |
| Group IV  | { | Serum agglutinates corpuscles of Groups I, II, and III. |
|           | { | Corpuscles agglutinated by no serum.                    |

Although he did not observe hemolysis as frequently or as consistently as agglutination, yet he believes that hemolysis never acts contrary to the laws of agglutination, as stated in the foregoing table.

Accordingly, if the reaction *in vivo* were the same as that in the test-tube, one would expect (from the above table) that patients belonging to Group I would give no reaction against any of the four different groups of corpuscles injected, because their serum agglutinates no corpuscles, and of course hemolyzes none.

Patients belonging to Group II might give a reaction with corpuscles from Groups I and III.

Patients belonging to Group III might give a reaction with corpuscles from Groups I and II.

Patients belonging to Group IV might give a reaction with corpuscles from Groups I, II, and III.

DETERMINATION OF AGGLUTIN GROUPS. Naturally, in order to test the above, it became necessary to obtain members of the four groups mentioned. Moss found that representatives of Groups II and IV were quite common, whereas Groups I and III were comparatively rare. In his report of a hundred group determinations he found the following percentages: Group I, 10 per cent.; Group II, 40 per cent.; Group III, 7 per cent.; Group IV, 43 per cent.

In our series, 45 individuals were examined before a Group I was found, so that we decided to extend these observations with the purpose of confirming Moss' findings. The results of determinations in 192 cases follow:

	Healthy.		III.		Total.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Group I . . .	3	5	10	8	13	6.7
Group II . . .	22	34	42	33	64	33.3
Group III . . .	4	6	16	13	20	10.0
Group IV . . .	35	55	60	46	95	50.0

Within reasonable limits, then, our results compare very closely with those of Moss, as regards the relative frequency of the groups, with the exception that Group III is more common than Group I; likewise, it is interesting to note that with the exception of Group III the percentages vary but slightly between healthy and diseased individuals, and a larger series of cases would probably diminish this discrepancy.

It is perhaps worth recording that the agglutination reaction of the various groups differs, as regards the rapidity with which the reaction takes place. Group IV, for example, must possess serum of extraordinary power, for complete agglutination occurs within five minutes after mixing the serum and the corpuscles. Group II, on the other hand, frequently cannot be recognized for fifteen

minutes to half an hour, and Group III requires still longer for positive identification. Group I agglutinates no corpuscles.

In determining the groups to which the patients belonged both the microscopic and macroscopic methods were employed.

**TECHNIQUE OF THE SKIN REACTION.** The technique employed by us in performing the skin test in the cases to be reported was as follows: On the day before the tests were to be made, 4 individuals were selected, 1 from each of the four groups, care being taken to exclude patients having syphilis or any other transmissible disease. Under aseptic conditions 15 c.c. of blood were removed from a vein of the forearm and immediately introduced into sodium citrate, to prevent clotting. It is important to wash out the syringe with sodium citrate before use, in order to prevent any hemolysis from water left in the syringe after boiling. The corpuscles thus obtained were centrifugalized, the supernatant fluid pipetted off, and the cells washed three times with normal salt solution. Strictly aseptic technique was observed throughout.

A 20 per cent. suspension of each set of corpuscles was then made and allowed to remain over night in the ice chest. They were then ready for injection, and were drawn up into sterile syringes previously washed out with normal salt solution.

The entire flexor surface of the forearm of the patient to be tested was rendered surgically clean. Five cubic centimeters of blood were taken from a vein of the patient's forearm with a needle and syringe, previously boiled and washed out thoroughly with sterile sodium citrate. The blood was introduced into a sterile tube, allowed to clot, and the clear serum removed with a capillary pipette,  $\frac{1}{2}$  c.c. of serum being placed in each of four test-tubes. Then  $\frac{1}{2}$  c.c. of a 5 per cent. suspension of Group I corpuscles was added to the serum in tube No. 1. One-half of a cubic centimeter of a 5 per cent. suspension of Group II corpuscles was added to the serum in tube No. II. Similar mixtures of the patient's serum and corpuscles were made with Groups III and IV. The tubes were shaken and allowed to remain in the thermostat for two hours at 36° C. Readings were then made for agglutination and hemolysis. The grouping was readily determined by noting the tubes in which agglutination had occurred. Hemolysis was observed in various grades. Even slight traces were noted, in order to furnish data for comparison with the skin reaction.

After removing the 5 c.c. of blood from the forearm for the test-tube reaction  $\frac{1}{3}$  c.c. of the corpuscle suspension of each of the four groups prepared the day before was injected subcutaneously into the forearm at points about 5 cm. apart. The injection should be given under the skin and not into it. A small bulla at once appears when the injection is properly given, which soon subsides, leaving a pin-point abrasion where the needle entered. When the skin itself is injected discoloration may appear immediately and may

cause confusion in interpreting the result. In selecting the site of injection, one should avoid superficial veins. It is advisable to give injections early in the day so that observation by daylight is possible. The corpuscles used were never more than twenty-four hours old.

Observations of patients were made four, six, and eight hours after injection. Our readings both of the skin reaction and of the test-tube controls were made independently by us, and our findings compared only after each series of experiments had been completed. In every case they were in entire accord.

Table I includes the diagnosis in each case, with the isohemolysin and isoagglutinin group to which each patient belongs. It then graphically compares, side by side, the reaction of the patient's serum upon the corpuscles of each group *in vivo* and *in vitro*, the former being the skin reaction and the latter the test-tube reaction. Thus we have the patient's serum acting on the four different groups of corpuscles in the body tissues and in the test-tube.

This table comprises 123 cases, 15 of which were examples of various types of carcinoma in which the diagnosis was verified by operation, autopsy, or microscopic examination; 1 unverified case of carcinoma; 3 cases of sarcoma; and 103 cases of normal individuals, and patients suffering from various ailments, including cardiopathies, pneumonia, gout, malaria, pellagra, amebic dysentery, dementia paralytica, nephropathies, cirrhosis of the liver, arthritides, hernia, idiocy, gangrene, morphinism, epilepsy, pernicious anemia, fractures, neurasthenia, syphilis, etc.

The results of this detailed report are compiled in Table II, which shows 60 per cent. positive reactions (against all four groups) in cases of carcinoma; 13 per cent. doubtful reactions; and 27 per cent. negative reactions. In cases other than malignant disease (103), 10 per cent. were positive; 2 per cent. doubtful; and 88 per cent. negative.

DISCUSSION OF THEORETICAL BASIS OF SKIN REACTION. We have been able to show conclusively in our series of cases that not infrequently a patient's serum possesses marked hemolytic power for one, two, or three kinds of corpuscles when tested outside the body in the test-tube, whereas the same serum acting against the same corpuscles *in vivo* produces no hemolysis whatever. As an instance of this phenomenon, we cite a case of pleurisy Group IV, which gave no reaction whatever in the body, but completely hemolyzed the corpuscles of Groups I, II, and III in the test-tube. There were 16 such examples in our series. This would seem to show that a reaction for carcinoma depending upon the test-tube hemolysis, as proposed by Crile, would be quite unreliable, since isohemolysis occurs frequently in normal individuals, as well as in persons with various non-malignant diseases.



TABLE I.—Result of Skin Reaction as Compared with Hemolysis in Vitro, Using Corpuscles from the Four Groups.

No.	Group.	Name.	Diagnosis	How made.	Corpuscles, Group I.		Corpuscles, Group II.		Corpuscles, Group III.		Corpuscles, Group IV.	
					Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.
1	..	Singer, H.	Adenocarcinoma, rectum	Operation	Positive reaction.		Group of corpuscles		used not determined			
2	II	Golinsky, G.	Carcinoma, breast	Operation	+	0	+	0	+	0	+	0
3	II	Carroll, H.	Carcinoma, uterus	Operation	+	0	+	0	+	0	+	0
24	I	—, C.	Sarcoma, arm	Operation	+	0	+	0	+	0	+	0
5	III	—, D.	Carcinoma, jaw	Operation	+	+	+	+	+	0	+	0
6	IV	Horwitz, B.	Carcinoma, breast (recurr.)	Operation	..	..	+	..	+	..	+	..
7	I	Bay View Hosp.	Carcinoma, stomach	Autopsy	0	0	0	0	0	0	0	0
8	IV	Bay View Hosp.	Epithelioma, face	Operation	+	0	+	0	+	0	+	0
9	I	Bay View Hosp.	Epithelioma, head	Microscopic	0	0	0	0	0	0	0	0
10	III	Bay View Hosp.	Carcinomatosis	Autopsy	+	0	+	0	+	0	+	0
11	..	Matthews, G.	Carcinoma, breast	Operation	+	..	+	..	+	..	+	..
12	..	Kimble, G.	Carcinoma, bladder	Operation	+	..	+	..	+	..	+	..
13	IV	Nelson, D.	Carcinoma, rectum	Operation	0	0	0	0	0	0	0	0
14	IV	Ryan, H.	Carcinoma, cervix	Operation	+	+	+	+	+	+	+	+
15	..	—, G.	Carcinoma, breast	Operation	+	+	+	+	+	+	+	+
16	..	Starkey, H.	Carcinoma, bladder	Microscopic	+	+	+	+	+	+	+	+
*17	IV	2d test case 8	Epithelioma, face	Operation	0	0	0	0	0	0	0	0
18	II	Bay View Hosp.	Carcinoma, tongue	Microscopic	0	0	0	0	0	0	0	0
19	IV	Thomas, F.	Carcinoma, stomach	Clinical mass	0	+	0	+	0	0	0	0
*20	II	Summers, D.	Sarcoma, leg	Operation	0	0	0	0	0	0	0	0
*21	II	Hines, D.	Sarcoma, neck	Operation	0	0	0	0	0	0	0	0
22	II	Bluet, D.	Chronic appendicitis and gallstones	Operation	0	0	0	0	0	0	0	0

TABLE I.—(Continued.)

Group.	Diagnosis.	Corpuscles, Group I.		Corpuscles, Group II.		Corpuscles, Group III.		Corpuscles, Group IV.	
		Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.
IV	Normal individual	+	0	+	0	+	0	+	0
II	Normal individual	0	0	0	0	0	0	0	0
IV	Normal individual, tested three times	0	....	0	....	0	....	0	0
II	Normal individual, tested two times	0	0	0	0	0	0	0	0
III	Hernia	0	0	0	+	0	+	0	0
IV	Hernia	0	0	0	+	0	+	0	0
II	Hernia	0	0	0	0	0	0	0	0
IV	Hernia	0	0	0	+	0	0	0	0
I	Hernia	0	0	0	0	0	0	0	0
IV	Hernia	0	0	0	0	0	0	0	0
I	Fracture	0	0	+	0	0	0	0	0
IV	Fracture	0	+	0	+	0	+	0	0
SPECIFIC INFECTIOUS DISEASES.									
IV	Pneumonia	0	0	0	0	0	0	0	0
I	Pneumonia	0	0	0	0	0	0	0	0
	Pneumonia	Negative reaction.		Group of corpuscles used		not determined.			
II	Influenza	Negative reaction.		Group of corpuscles used		not determined.			
I	Rheumatic fever	0	0	0	0	0	0	0	0
IV	Rheumatic fever	0	0	0	0	0	0	0	0
II	Malarial fever	0	+	0	+	0	+	0	0
IV	Malarial fever	0	0	0	0	0	0	0	0
III	Malarial fever	0	0	0	0	0	0	0	0
IV	Syphilis	Negative reaction.							
II	Syphilis	0	0	0	0	0	0	0	0
II	Syphilis	+	0	+	0	+	0	+	0
I	Syphilis	0	0	0	0	0	0	0	0
	Syphilis	0	0	0	0	0	0	0	0
I	Tabes dorsalis	Negative reaction.							
	Spastic paralysis—lucetic (?)	0	0	0	0	0	0	0	0
	Gonorrheal arthritis	Negative reaction.							

TABLE I.—(Continued.)

Group.	Diagnosis.	Corpuscles, Group I.		Corpuscles, Group II		Corpuscles, Group III.		Corpuscles, Group IV	
		Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.
II	Tuberculosis, pulmonary	0	+	0	0	0	+	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
II	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
IV	Tuberculosis, pulmonary	Negative	reaction.						
IV	Tuberculosis, pleural effusion	0	0	0	0	0	0	0	0
IV	Tuberculosis, fibrinous pleurisy	0	+	0	+	0	+	0	0
II	Tuberculosis, larynx	+	+	+	+	+	+	+	+
IV	Tuberculosis, osteomyelitis	+	0	+	0	+	0	+	0
CONSTITUTIONAL DISEASES.									
II	Diabetes	0	0	+	0	+	0	+	0
II	Diabetes	+	0	+	0	+	0	+	0
IV	Diabetes	+	+	+	+	+	+	+	+
	.....	0	+	0	+	0	0	0	0
	Acute gout	Negative	reaction.						
III	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	0	+	0	0	0	0	0
IV	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	+	0	0	0	+	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease, tested twice	0	0	0	0	0	0	0	0
III	Cardiac disease	0	0	0	0	0	0	0	0
II	Endocarditis	0	0	0	0	0	0	0	0
IV	Endocarditis, purpura	0	0	0	0	0	0	0	0
	Endocarditis, purpura	Positive	reaction.	0	0	0	0	0	0



TABLE II.

	Positive. Per cent.		Negative. Per cent.		Doubtful. Per cent.		Total.
Verified cancer cases . . . . .	9	60	4	27	2	13	15
Doubtful cancer cases . . . . .	..	..	1	..	..	..	1
Verified sarcoma cases . . . . .	1	33 $\frac{1}{3}$	2	66 $\frac{2}{3}$	..	..	3
Non-malignant cases . . . . .	10	10	91	88	2	2	103
Cancer case . . . . .	..	..	..	..	..	..	1
Once positive (No. 8)							
Once negative (No. 17)							
Grand total . . . . .							123

In Case No. 20 the test was made after amputation.

*Vice versa*, we have had cases showing marked positive reactions in the body whose sera showed absolutely no hemolytic power against the same corpuscles when tested *in vitro*. As an instance of this reverse phenomenon, we cite a case of sarcoma of the arm which gave a strong positive reaction against each of the four groups of corpuscles, *in vivo*, but no hemolysis against the same corpuscles in the test-tube. Elsberg, Neuhoﬀ, and Geist<sup>10</sup> explain the reaction as follows:

"If normal blood cells are injected under the skin of a patient whose serum is hemolytic, fresh quantities of hemolysin would be continually brought to the cells by the circulating blood and lymph, and, therefore, even if the amount of hemolysin in the blood of the patient was very small, the injected cells might, nevertheless, be hemolyzed. Every organic substance which was liberated by the destruction of the injected red cells would enter the tissues and there have its effect. The hemoglobin and other substances which had been set free might cause a local change in the tissues at the site of the injection. If blood cells are injected under the skin of a normal individual, they are broken up and carried off by the body cells and fluids; the condition of affairs under the skin of a patient whose blood serum contains free hemolysins would be an entirely different one because a different process was taking place."

Elsberg, Neuhoﬀ, and Geist's hypothesis that the reaction may be due to a larger quantity of hemolysin containing serum constantly bathing the injected cells does not explain all the facts, since some sera show strong hemolytic properties *in vitro* and none *in vivo*. So it seems justifiable to assume that there may be two hemolysins or hemolytic processes, one of which is met with in the body in some cases, especially carcinoma; the other of which occurs in test-tube reactions when the serum of normal or of diseased persons is allowed to act on red blood cells. Our small

series of about 400 injections and 400 test-tube controls shows no relation existing between these two types.

Accordingly, our expectation that the normal isohemolysis would account for an appreciable number of the positive skin reactions has not been realized. In none of our cases showing an outspoken skin reaction, was there any relation existing between the intensity of the reaction and the isoagglutinin or hemolysin grouping of the corpuscles.

However, the utilization of the four groups of corpuscles for injection has revealed the significant fact that it is not a matter of indifference as to the type of corpuscles selected for the test. Our series of cases shows several instances in which the reaction was positive about one or two of the corpuscle groups and negative at the site of injection of the others. Such cases were considered negative. Only those were called positive in which all four types of corpuscles were affected. So it is conceivable that the injection of simply one type of corpuscles, the group of which is unknown, might lead to an erroneous deduction. In spite of this, however, there appears to be one group of corpuscles, namely, Group IV, which might be utilized for the reaction with reasonable reliability. It will be remembered that the corpuscles of Group IV are neither agglutinated nor hemolyzed by any sera *in vitro*. In our entire series of 124 cases, in which the four types of corpuscles were injected subcutaneously, not a single instance was observed in which the corpuscles of Group IV gave a positive reaction without the corpuscles of Groups I, II, and III also showing a positive reaction.

Accordingly, from the above results, if a positive reaction were obtained about the site of injection, of corpuscles from Group IV, it would be *ipso facto* evidence that corpuscles from Groups I, II, and III would likewise have been hemolyzed. On the other hand, if a negative reaction were the result of such an injection the test would be considered negative, even if corpuscles from Groups I, II, or III would have given a positive reaction.

It is not justifiable, however, to reach a definite conclusion on this point from the study of so few cases. The action of Group IV corpuscles should be observed in an extended series of cases where all four types are injected. If this point is substantiated, then the injection of Group IV corpuscles alone will prove sufficient for the reaction.

Perhaps it should be noted that our decision to consider a skin reaction positive only when all four groups of corpuscles are hemolyzed is an arbitrary one, since further study may show that the different groups have different powers of resistance to the sera of cancer patients.

After reviewing this work we feel reasonably confident that our main object has been accomplished; namely, placing the carcinoma

skin reaction on a conservative scientific basis. The actual clinical value of the test is by no means determined, but we are of the opinion that it can be determined now with accuracy. Many problems in connection with this reaction, bearing upon its aid in the diagnosis of malignant disease are now open for solution.

1. Whether a positive reaction can be secured in early cases of malignant disease, where the clinical diagnosis is quite doubtful, thus permitting early operative interference.

2. Whether the reaction can be utilized as an index of cure after complete radical operations; and how soon the reaction disappears after operation, provided it has been positive before.

3. Whether the reappearance of a positive reaction two or three years after operation would be indicative of recurrence.

These and many other problems are of great interest, but can be determined only after large series of cases have been tested with repeated injections over a long period of time. But we feel that as a result of this work, such problems can now be readily solved and the true diagnostic value of this reaction judged precisely.

CONCLUSIONS. 1. The test is certainly not specific for carcinoma. We have found it positive in somewhat more than half of patients suffering from cancer (60 per cent.) and negative in a large majority of patients showing other forms of disease (about 89 per cent.) It may prove to be another help in the diagnosis of cancer, and its value is sufficient to warrant the application of the test and study in large series of cases.

2. Apparently no connection exists between a positive skin reaction and hemolysis in the test-tube. The test-tube method is of questionable value.

3. The grouping to which the corpuscles employed for injection belong is not a matter of indifference but one of considerable importance.

4. We are not prepared to speak as to the special value of the reaction in differentiating early carcinoma and borderline tumors, or as to its absence in advanced cases.

5. A positive reaction is of much greater significance than a negative one. If the reaction is positive, the patient very probably suffers from cancer; if, however, it be negative, cancer cannot be excluded.

We desire to express our appreciation of the constant interest and advice of Dr. Moss, under whom this work was completed, and to acknowledge further the kindness of Drs. Barker, Halsted, and Finney in allowing us the privilege of their cases; to thank Drs. Sladen, Remsen, and Cullen and other members of the resident hospital staff of the Johns Hopkins Hospital for assisting us in obtaining suitable cases; likewise Dr. Boggs for placing at our disposal the patients at the City Hospital, Bay View.

## REVIEWS

---

COLLECTED PAPERS BY THE STAFF OF ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA, 1910. Pp 633; 291 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

THE second of these volumes of bound reprints, emanating from the "Mayo Clinic," comprises those papers published during the year 1910, and makes as large a collection as the first volume which included the papers from 1905 to 1909. If the increase in productiveness continues at a similar rate it will be necessary to issue several volumes yearly. But the material available is so immense, and so pressing is the duty which it entails of making available anything of value which can be learned from the experience gained, that no doubt the chiefs of the clinic feel like Paul when he exclaimed, in extenuation of his insistent teaching, "Woe is me if I preach not the gospel."

More than a score of authors are represented, and more than half the volume is filled with papers dealing with the surgery of the alimentary canal. Genito-urinary subjects occupy over a hundred pages, the ductless glands about fifty, and the head, neck, and extremities about twenty-five pages. The volume closes with a series of miscellaneous addresses, notes of travel, etc., which are well worth perusal.

A volume of such miscellaneous subject matter as this does not lend itself readily to reviewing. Moreover, the articles have appeared in current journals, and have already reached their audience. There is much information embodied which it is convenient to have at hand for reference, though the volume contains few really noteworthy contributions either to the science or art of surgery. Critically speaking, the best of these contributions are those dealing with the surgery of the esophagus, and with the relation of obliteration of the appendix to carcinoma. The studies of hypernephroma are also of interest. As much cannot be said of the lengthy and profusely illustrated articles on the pathology of the stomach and gall-bladder, which embrace nothing of particular interest or novelty. The arguments advanced against the non-operative and in favor of the "open" treatment of fractures are not supported by any clinical evidence; recent fractures



do not appear to enter St. Mary's Hospital, and the reports of bad results obtained elsewhere are not convincing either of the inadequacy of proper non-operative treatment or of the benefits to be secured by operation at the hands of the Rochester surgeons.

The volume is not so well edited as was the first; but without this comparison it would still pass for a well-edited volume. The typographical errors are few; among others of less import may be mentioned *leukæmia* for *leukopenia* (p. 460). The arrangement of articles is judicious, and the bibliographic index seems complete and accurate. The index of subjects, however, suffers from over-completeness; when one looks up a definite topic he is very apt to find half a dozen references to pages where the subject is barely mentioned, and only one reference (not distinguished in the index from the others) to the one place where the topic is fully discussed.

A. P. C. A.

---

A MANUAL OF CLINICAL DIAGNOSIS BY MEANS OF LABORATORY METHODS. FOR STUDENTS, HOSPITAL PHYSICIANS, AND PRACTITIONERS. By CHARLES E. SIMON, B.A., M.D., Professor of Clinical Pathology and Experimental Medicine at the College of Physicians and Surgeons; Pathologist to the Union Protestant Infirmary and the Hospital for Women of Maryland; Clinical Pathologist to the Mercy Hospital of Baltimore, Maryland. Seventh edition; pp. 778; 168 illustrations and 25 plates. Philadelphia and New York: Lea & Febiger, 1911.

THE first edition of this book, the pioneer work on clinical diagnosis in America, appeared a little over fifteen years ago. The new seventh edition has recently been published. This enviable record, all the more remarkable when we consider the technical character of the book, is evidence not only of the continued popularity of Simon's work, but also shows an increasing appreciation on the part of the medical profession of the value of clinical pathology.

In the new edition, the work has undergone a thorough revision, the most noteworthy feature of which is the division of the text into two parts. Part I, which includes about two-thirds of the book, is technical and deals with the various clinical examinations. Part II, which is clinical, is entirely new and has added much to the value of the book. In this portion, the findings in the blood, urine, feces, etc., peculiar to a given disease, are briefly discussed, thus enabling the student to more readily interpret laboratory findings.

In order to accomplish this change without increasing the size of the book, certain of the less essential portions of the earlier edi-

tions have been condensed or omitted. For example, in the new edition the chapters on the secretion of the mammary gland, vaginal discharges, and opsonins that appeared in the preceding edition, have been omitted, and the chapter on secretions of the mouth has been materially shortened. On the other hand, the most important features of these chapters are included under the various diseases in Part II of the present edition.

It is unnecessary to enumerate the many alterations and modifications that have been made throughout the older technical portion of the book. In general, the arrangement and treatment of the subject matter is similar to that found in the last edition. Tests and reactions which are no longer in general use have been replaced by modern methods. In this connection attention should be called to certain additions, the most notable of which are the admirably clear account of the Wassermann reaction and its technique, including Noguchi's modification, which concludes the chapter on blood; the addition to the chapter on the urine of the phenolsulphonephthalein test for the determination of renal insufficiency and the Noguchi butyric-acid test as applied to the cerebrospinal fluid. Although there are no important omissions, Lange's test for acetone in the urine and Rivalta's reaction as a means of differentiating between transudates and inflammatory exudates might with advantage have been included.

For the practitioner and student who desires a clear, concise, and reliable treatise on laboratory examinations and their significance, the book is indispensable. In its present form Simon's book stands easily the foremost work in English on clinical pathology.

G. M. P.

---

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO, APRIL, 1912. Pp. 156; 38 illustrations. Philadelphia and London: W. B. Saunders Co., 1912.

THE April number of this magazine contains a great many interesting disquisitions on topics in widely varying fields of surgery. Those dealing with bone and joint work naturally attract most attention, as they occupy the major portion of this issue, as they did of the first, and are more fully illustrated by skiagraphs and photographs than are the remarks on other matters.

The publishers insert an apologetic note, explaining that the errors of omission in the first issue were due to the haste involved in publication. They make no mention of faults of commission, but promise to do better in the future. Indeed, the second number gives evidence of having received some editorial revision, and we have noticed comparatively few misprints. According to the pub-

lishers' original announcement it is implied that Dr. Murphy has nothing to do with seeing the work through the press, so such errors as there are cannot be chargeable to him. His own part in the work appears to be confined to the spoken word; and it is unfortunate, or perhaps rather fortunate, that this does not exert on the profession the same force it would if they knew that what was spoken perhaps in haste was revised and corrected at leisure. "Litera scripta manet," and perhaps Dr. Murphy may be sorry to see in bold print assertions which are open to adverse criticism. For instance, in the account of Volkmann's contracture Dr. Murphy is made to assert that this lesion *always* is the result of badly applied dressings, and that it *never* occurs unless dressings have been applied. This statement is flatly contradicted by several cases on record, in which Volkmann's contracture followed an injury in which no dressing whatever had been applied. So, too, the unqualified assertion that there never are any nerve lesions in these cases is one that will not bear too close scrutiny. It is scarcely conceivable that such wild statements could pass the author's editorial blue pencil unchallenged, though he might make them during a clinical lecture in the endeavor to enforce an important lesson. And after all the charm of this series of publications (and it is great) lies in this very fact, that a great teacher is by this means constantly enforcing very important clinical lessons. The reviewer, with many other readers, at home and abroad, learns much from Murphy's clinics, and is duly grateful; but he takes some of the statements "cum grano salis." A. P. C. A.

---

LIPPINCOTT'S NEW MEDICAL DICTIONARY: A VOCABULARY OF THE TERMS USED IN MEDICINE, DENTISTRY, VETERINARY MEDICINE AND THE ALLIED SCIENCES, WITH THEIR PRONUNCIATION, ETYMOLOGY AND SIGNIFICATION, INCLUDING MUCH COLLATERAL INFORMATION OF A DESCRIPTIVE AND ENCYCLOPÆDIC CHARACTER. By HENRY W. CATTELL, A.M., M.D., Editor of *International Clinics*. Second edition. Pp. 1108. Philadelphia and London: J. B. Lippincott Company, 1911.

THE first edition of this work was reprinted and now appears in its second edition within a year, thus giving good evidence of the value of the work and the appreciation of it by the public. It may not be generally known that this was the first medical dictionary to contain veterinary as well as medical terms; and the first to use capital and small letters, making it a guide to capitalization. It was also the first to indicate the B. N. A. terms and the drugs that are official in the Pharmacopœia.

In the present edition, over five thousand additions and changes have been made, seventy-one new illustrations have been added, a number of old ones have been withdrawn, and five hundred new words, which appear for the first time in a dictionary, have been inserted. The work is unusually complete and comprehensive, without being bulky. The definitions are clear and concise and, where necessary, are appropriately illustrated. The book is printed on good paper, bound in flexible leather, and has a thumb-index. It is in every particular to be recommended as a valuable book of reference for students and practitioners. F. H. K.

---

A MANUAL OF GYNECOLOGY. By THOMAS WATTS EDEN, M.D., C.M. Edin., F.R.C.P. Lond.; F.R.C.S. Edin., Obstetric Physician with Charge of Out-patients, and Lecturer on Midwifery and Gynecology, Charing Cross Hospital, etc. Pp. 632; 272 illustrations. Philadelphia: P. Blakiston's Son & Company, 1911.

THE author states that he has written this manual to provide for students and general practitioners a complete but not an exhaustive account of the diseases of women in their pathological and clinical aspects. This object he has attained with remarkable success.

The anatomy and physiology of the female pelvic organs occupies the first portion of the book. The uterus at different periods of life is concisely and clearly described. The ovary and its various tissues and the parovarium, receive adequate description, and our knowledge concerning ovulation and the internal secretion of the ovary is concisely stated. An exact description of menstruation and the menopause concludes Part I.

In Part II, the author describes methods of examination. He employs most often Ferguson's and Sims' specula. Although the dangers which attend the use of the sound are described, it is evidently employed by the author, and illustrations are given which show its application, guided by touch and not by sight. Many American gynecologists would hesitate to use the sound in this manner, and it is probably the least employed of all gynecological instruments at present in America.

Certain prominent gynecological symptoms next receive attention. The various discharges from the genital organs are concisely described and also the different sorts of pain referred to this region. Disturbance of micturition, and the causes producing sterility, are also treated.

In considering disorders of menstruation, he classifies amenorrhea as primary and secondary, regarding the first as usually a symptom

of imperforate hymen or atresia; and secondary amenorrhea as a symptom and not a disease.

Dysmenorrhea he classifies as spasmodic or congestive, and describes intermenstrual pain as an added complication. In severe cases of spasmodic dysmenorrhea, when all else has failed, if operation is to be performed he would prefer to remove the uterus, leaving the ovaries. Congestive dysmenorrhea he considers a symptom of pelvic disease.

The author devotes considerable space to morbid conditions of the uterus, beginning with displacements. He would address treatment, in antelexions, not to the correction of the abnormal uterine angle, but to the alleviation of the causal conditions when practicable. In backward displacements the uterine sound again figures as an instrument to be employed for replacing the uterus. Eden evidently does not practice manual replacement in the knee-chest posture, which we have found the most valuable of all methods. The Hodge and Albert Smith pessary are described and their uses illustrated. Prolapse is treated at considerable length, and various pessaries are discussed.

Endometritis receives an extended description. The acute form of exfoliative endometritis he believes to depend upon systemic infection, the local condition not requiring treatment. The chronic form he believes to be practically incurable. Under the head of fibrosis uteri he describes chronic metritis. In cases which resist general treatment he would remove the uterus, saving the ovaries if healthy.

The author gives an excellent account of fibroid tumors of the uterus, the changes which sometimes develop in them, and the part which they play as a complication of pregnancy. He recognizes that not all fibroids require treatment, but believes that surgical treatment should not be delayed when the tumor is increasing rapidly in size, and is accompanied by pain; when the fibroid which has been quiescent becomes troublesome in any way after the menopause; and when palliative treatment fails to control bleeding and there is advancing anemia. Hysterectomy with conservation of the ovaries when healthy, he believes, will be found most generally useful.

Malignant growths of the uterus are fully described. He advises the radical operation whenever there appears a reasonable hope of the possibility of its performance. Even though recurrence should follow radical operation, he believes life may be prolonged, and the recurrent disease may be much less distressing.

Under the head of sarcoma of the uterus, chorion epithelioma is described.

Under morbid conditions of the ovaries Eden regards ovarian neuralgia as a neurosis not dependent on structural changes. Dis-

placements of the ovaries, when they cause pain and distress, may usually be cured by operation.

The author describes and fully illustrates the various forms of ovarian cyst, and also cancer of the ovary. He places ovarian sarcoma under the head of connective-tissue tumors.

Tubal pregnancy is described as a morbid condition of the Fallopian tubes, in a section devoted to inflammatory diseases, newgrowths, and congenital abnormalities of the tubes. Tuberculous pyosalpinx and hematosalpinx are included under inflammation of the tubes and ovaries.

In gonorrheal infection Eden has obtained good results by the use of the vaccine in large doses, from 100,000,000 to 500,000,000 organisms injected once a week under the skin of the arm or thigh.

In dealing with tuberculous infection of the pelvic viscera he holds that radical operation should not be performed unless pus is present, if tuberculous peritonitis is found. When the disease is limited to the pelvic organs radical operation is indicated.

In the treatment of ectopic gestation he recommends removal of the gravid tube or ovary without delay by abdominal section, if a diagnosis can be made before rupture.

Diseases of the vagina, vulva, and urethra, are clearly described with abundant illustrations. Malformations of the vagina and uterus are briefly considered.

The concluding section of the work is a description of the technique of the various operative procedures. In preparing patients for operation, Eden emphasizes that attention should be given to the condition of the mouth. Carious or suppurating teeth should be removed, and the mouth disinfected as thoroughly as possible. The presence of menstruation does not, he believes, in any way complicate operative procedures, or prejudice convalescence, and it is unnecessary to postpone operation on this account.

In performing Wertheim's operation, Eden has modified Wertheim's vaginal clamp to secure a better grasp of the tissues throughout the entire length of the clamp. The advantages and disadvantages of the vaginal method are clearly stated, and the operation is illustrated. Ventrofixation is advised in backward displacements of the uterus, and shortening of the round ligaments by the Alexander-Adams' method is practised where the ligaments are strong enough to warrant their employment. It is thought that a preliminary six weeks' course of massage and physical exercises for strengthening the abdominal wall may improve the results in the various suspensory operations.

The book concludes with a section devoted to the after-treatment of major operations and a brief section on therapeutic notes.

While this work will not give to the reader a minute and exhaustive discussion of so large a subject, it presents in convenient compass a clear and concise description of modern gynecology.

It will be found especially useful as a hand-book for the practitioner, who can readily secure the practical points in a given case and decide upon its treatment. It will be useful to the specialist as a concise summary of modern methods. The illustrations are clear and largely original.

E. P. D.

A POCKET MEDICAL FORMULARY. By E. QUIN THORNTON, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College, Philadelphia. Tenth edition. Pp. 288; containing over 2000 prescriptions. Philadelphia and New York: Lea & Febiger, 1912.

THAT the cry of the therapeutic nihilists goes largely unheeded by the general practitioner is shown by the recent appearance of the tenth edition of the *Pocket Medical Formulary*. This eminently useful little volume, bound in flexible leather, and of a size suitable for the pocket, is arranged so as to be available for instant reference.

It begins with comparative tables of apothecaries' weights and measures and the metric system, following this are given the important incompatibilities, poisons and their antidotes, and a comprehensive alphabetical list of drugs and their doses.

The bulk of the book comprises a surprisingly complete list of diseases and important symptoms, alphabetically arranged, under each of which are given the prescriptions and other methods of treatment best adapted to the management of the condition in question. In every instance the suggestions as to treatment embody that which is best and most scientific in modern therapeutics. The formulæ furnished are for the most part models of simple, careful prescription writing, and contain only drugs that are official in the several pharmacopœias or have been tested and approved by the Council of Pharmacy and Chemistry. The value of each formula is decidedly enhanced by giving under it the indications for its use. It is gratifying to find that the "shot-gun" prescription is noticeably absent, and that proprietary remedies find no place in the book.

That this new edition is truly up to date is evident when we find salvarsan and its administration discussed under syphilis; staphylococcus vaccine mentioned as an important method of treating abscesses, furunculosis, and acne; antistreptococcic serum advised in pyemia; and human blood serum recommended in the treatment of hemorrhage and purpura.

A book such as the *Formulary* must of necessity have certain limitations and will perhaps call forth unfavorable comment from those who are opposed to furnishing practitioners and students

with stock prescriptions. Nevertheless, it has its field of usefulness, since it affords, not to the younger clinician alone, but also to his more experienced colleague, a ready means of acquiring reliable, safe, and legitimate therapeutics. Moreover, it is not too much to assert that the more general use of a book of this kind would aid many a practitioner to do his own prescribing and, as a consequence, would materially lessen the hold which the detail man with his proprietary remedies has today upon the profession.

G. M. P.

---

A HANDBOOK OF MEDICAL DIAGNOSIS FOR THE USE OF PRACTITIONERS AND STUDENTS. By J. C. WILSON, A.M., M.D., Professor of the Practice of Medicine and Clinical Medicine in the Jefferson Medical College, and Physician to its Hospital. Third edition, 1438 pages, 418 illustrations, and 14 full-page plates. Philadelphia and London: J. B. Lippincott Company, 1911.

THE first edition of this work was published in 1909. It appeared in its second edition, with minor changes and a few additions, in 1910; and is now presented in its third edition, after a complete and thorough revision. The advances in the subject of clinical medicine have been so rapid along certain lines during the last few years that frequent and often extensive revisions of works on this subject are necessary, in order to keep abreast of the best thought of the times.

The subject matter is divided into four parts: (1) Medical diagnosis in general; (2) the methods and their immediate results; (3) symptoms and signs; (4) the clinical applications. This arrangement has been chosen with a twofold purpose: That "within the compass of a single book, clinical phenomena, on the one hand, and, on the other, those complexes of clinical phenomena that constitute diseases, are brought into correlation in such a manner that the practitioner who seeks information upon an obscure case may at once turn to the discussion of the methods available to clear it up; and the student may find the definite clinical applications of the same methods and their results in descriptive medicine." The work really combines the essentials of medical topography, physical diagnosis, clinical pathology, and the practice of medicine. Treatment is, of course, entirely omitted.

In these days of multiple publication, the advisability of combining in one volume so many different but allied subjects may be rightly questioned. In such an attempt not only is each subject apt to suffer in some of its essential details, but there is bound to be considerable repetition. Be that as it may, the present work fulfills its mission, and should serve as a valuable book of



reference for both student and practitioner. The arrangement of the individual parts of the book is good, although at times the subdivision of the subject matter is a little bewildering. This is particularly true of the section on symptoms and signs. In the effort to avoid the discussion of moot and unsettled questions, the author might be accused of not having included some of the more recent theories and advances in the subject, that are apparently well worked out. This, however, is probably a safe failing in these days of rapid progress, and adds much to the practical value of the work. The free use of the metric system is to be commended, especially as its universal adoption is being urged in medical schools.

The illustrations are fairly numerous and, with some few exceptions, good. The plates are unusually good, especially those of the blood, malarial parasites, and vaccination. The index is full and complete, and makes reference to the many and varied subjects easy.

With these few criticisms, the work is reasonably complete, up-to-date, practical, and a valuable addition to our works on medical diagnosis.

F. H. K.

MANUAL OF THE DISEASES OF THE EYE FOR STUDENTS AND GENERAL PRACTITIONERS. By CHARLES H. MAY, M.D., Chief of Clinic and Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department, Columbia University, New York, 1890 to 1903; Attending Ophthalmic Surgeon to the Mt. Sinai Hospital, New York, etc. Seventh edition; pp. 407; 362 illustrations, with 62 colored figures. New York: William Wood & Co., 1911.

OF this book there have been six American editions since 1900; three British, two each of German, Italian, French, and Dutch translations, three Spanish, and one Japanese. This is surely a remarkable record. Such a book is interesting from that fact alone, and challenges study, if only to discover the reasons for such extraordinary success; of these reasons, two are of special moment—the numerous and excellent illustrations, which almost give it the place of a special atlas, and secondly, the circumstance that the author has selected wisely and tells what he has to say in clear language. It is not making an extravagant claim to assert that modern ophthalmology, so far as this can be done in a limited number of pages, is set forth in this small volume. The book has kept pace with the newer developments of the subject without becoming unduly large, and thus losing its original purpose as a concise manual. The book deserves the success it has gained in its competition with numerous works having a similar form and purpose in the ophthalmic literature of the principal nations of the world.

T. B. S.

CHOLERA AND ITS TREATMENT. By LEONARD ROGERS, M.D., F.R.C.P., F.R.C.S., B.S., I.M.S., Professor of Pathology, Medical College, Calcutta. Pp. 236; 16 illustrations and 12 tables. London: Oxford University Press, 1911.

ALTHOUGH this book appeared at a time when cholera was particularly active, the coincidence was purely accidental, for it was planned and commenced three years ago. The work consists of an effort to combine the "accumulated knowledge and experience of the last century with the system of treatment based on the writer's researches on the blood and circulatory changes in cholera which have recently resulted in a very great reduction of the death rate among cases treated in Calcutta and elsewhere in India." The author has made an extended study of the disease, and has carefully gone over the literature. The historical sketch, making up the first chapter, is particularly interesting, and is much simplified by a series of maps showing the paths of extension of the various epidemics. In this chapter also the author traces clearly the conditions in each epidemic, which finally led up to the discovery of the causative agent of the disease and its main characteristics. Of particular interest are the discussions on uremia in Chapter IV, blood changes, in Chapter V, and their bearing on prognosis and treatment, and the whole of Chapter VI on treatment. The latter, occupying about 75 pages, is of interest from an historical standpoint, but particularly so because of the modern conception of the subject. Considerable space has been devoted to a discussion of the use of intravenous injections of hypertonic saline solution, a method of treatment original with the author and one followed by a mortality considerably lower than that of any other method so far proposed.

The entire subject is well covered in a most interesting and readable book. The inclusion in the book of a list of the more important works on cholera adds considerably to the value of the book to any one making a study of cholera from any standpoint.

F. H. K.

---

TEXT-BOOK OF OPHTHALMOLOGY. By DR. ERNST FUCHS, Professor of Ophthalmology in the University of Vienna. Authorized Translation from the twelfth revised and greatly enlarged German edition, with numerous additions by ALEXANDER DUANE, M.D., Surgeon, Ophthalmic and Aural Institute, New York. Fourth edition. Pp. 989; 441 illustrations. Philadelphia and London: J. B. Lippincott Company, 1911.

As Fuch's Ophthalmology is about as well known to students of that specialty as Gray's *Anatomy* is to the general profession,

the reviewer can only point out some salient features in which the successive editions as they appear differ from their predecessors. That a treatise upon ophthalmology should pass through twelve editions in a little more than twenty years in the language in which it was written, not to mention the various translations, is unique in the history of ophthalmic literature, and indicates most pointedly what manner of impression the work has made. Among the qualities which have made the work so deservedly popular, three are preëminent: Judicious selection, clearness of presentation, and sanity of judgment. These are the triad of qualities, in truth, upon which excellence of every scientific treatise is primarily based. While clearness has not always been a characteristic of German writers, this quality has been present in the original from the first, and one of the great merits of the English translator is that he has been able to reproduce the same in English.

Among the important new additions to the work is an introduction of sixty-seven pages which deals with the general physiology, pathology, and therapeutics of the eye—all set forth with a lucidity which is so often wanting in the usual presentation of certain of these important topics. While in an earlier German edition (the fourth) the important subjects of disturbances of motility, and anomalies of refraction and accommodation were given one hundred and twenty-six pages, the present edition devotes one hundred and sixty-seven larger and more closely printed pages to the same subjects. It is these two chapters that the translator has annotated most largely, as indeed might be expected from the successful attention which Dr. Duane has for a long time been devoting to these cardinal divisions of ophthalmology. As in previous editions the translator's notes are enclosed in brackets leaving the author's text undisturbed. No mention appears to be made in the original text of certain of the newer developments of ophthalmology, such as the indications of arteriosclerosis in the retinal vessels, Lagrange's operation in glaucoma, Smith's extraction in the capsule, the therapeutic use of salvarsan, Tscherning's hypothesis of accommodation, etc. These are all briefly referred to in the translator's notes. In the preface to the first German edition the author insists upon the far greater importance from a practical point of view of the diseases of the anterior portion of the eye, like his illustrious predecessor Arlt. He accordingly devotes comparatively little attention to the affections of the deeper structures, choroid, retina, and optic nerve. In the original preface this is justified largely on account of the little success from therapeutics.

The work from a physical standpoint has about reached its limit. If further editions are to be made it will probably have to appear in two volumes. The mechanical execution is good. The illustrations add much to the text. Some of the colored plates, however, might be improved.

T. B. S.

PRACTICAL LESSONS IN NURSING. FEVER NURSING: DESIGNED FOR THE USE OF PROFESSIONAL AND OTHER NURSES, AND ESPECIALLY AS A TEXT-BOOK FOR NURSES IN TRAINING. By J. C. WILSON, A.M., M.D. Visiting Physician to the Hospital of the Jefferson Medical College and the Pennsylvania Hospital; Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College, Philadelphia. Sixth edition; pp. 259; 28 illustrations. Philadelphia: J. B. Lippincott Company, 1911.

THIS book contains seven chapters dealing with fever nursing in general; the continued fevers; the periodical fevers; the eruptive fevers; and fevers with marked local manifestations.

THE fact that the book has lived since 1887, and has gone through six editions, shows plainly enough that it possesses unusual value. While designed for the use of nurses, it is one of the few books on nursing that is of equal value to both nurse and physician. The instruction covers that part of the successful treatment of fevers that is so often vague in the physician's mind—the exact details of proper nursing. The book should be of particular value to those physicians who are not always so fortunate as to have properly trained nurses on whom to depend, and who must, therefore, bear the burden of both nurse and physician. From beginning to end the book is well written, interesting, and valuable.

W. G. T.

HANDBUCH DER GESAMTEN MEDIZINISCHEN ANWENDUNGEN DER ELEKTRIZITÄT EINSCHLIESSLICH DER RÖNTGENLEHRE. By PROF. DR. MED. H. BORUTTAU, PROF. DR. MED. L. MANN, PROF. DR. MED. M. LEVY-DORN, and PROF. DR. MED. P. KRAUSE. Second volume, first half; pp. 409; 15 illustrations. Leipzig: Dr. Werner Klinkhardt, 1911.

THIS is the first half of the second volume of this monumental work. The first volume was reviewed in a previous issue. The appearance of this work has been delayed somewhat because it was found that it would be necessary to divide it in two parts. The first, which is here reviewed, consists only of the diagnostic points of the different nervous diseases, and the second, which is to appear shortly, will consist of the therapeutic application of electricity to these diseases. A third volume is to appear in the course of time.

IT is impossible to review minutely a book of this kind. Suffice it to say that it is by all means the best exposition of electricity in medicine ever published, and is a work such as it is only possible to have been written by German authors.

T. H. W.

A MANUAL OF NURSING. By MARGARET FRANCES DONAHOE, Formerly Superintendent of Nurses, and Principal of Training School, Philadelphia General Hospital. Pp. 489; 52 illustrations. New York and London: D. Appleton & Co.

IN a manual of nursing it is always difficult to decide just where the line shall be drawn between the knowledge necessary for the nurse and that properly in the province of the physician. The two fields necessarily overlap widely, and in order that the best work may be done by either physician or nurse, each must have considerable general knowledge of the province of the other.

The manual before us is designed for the needs of the nurse in training. The instruction on all matters pertaining strictly to nursing is clear, concise, and accurate. The methods are excellent, the directions easily followed.

The instruction on matters overlapping the province of the physician would be open to criticism in places for vagueness and inaccuracies were this a manual intended for the instruction of medical students. For the needs of the pupil nurse, however, this field has been covered amply and in general with commendable accuracy.

Among the many subjects considered in the *Manual* particular mention should be made of the chapters on the duties of the nurse in a hospital; personal care of the patient; food, its ingestion and assimilation; the administration of medicines; observation of symptoms; the theory of asepsis and antisepsis; wounds; bandaging; emergencies; venereal diseases in women and children; care of the eye, ear, nose, and throat; nursing typhoid fever; the nursing of the insane, and of contagious diseases; the nursing of infants and young children; the giving of anesthetics, and operating room technique.

As is usual in first editions, typographical and grammatical errors have in places been overlooked. These do not detract from the value of the book as a whole, and, as there is much that is good in the book, will undoubtedly be corrected in future editions.

W. G. T.

ANOMALIE KINDER. Dr. med. L. Scholz, Direktor der Provinzial Irren- und Idiotenanstalt in Kosten (prov. Posen). Pp. 442. Berlin: S. Karger, 1912.

THIS is an excellent presentation of the developmental and psychopathic conditions found in children. The author has had a wide experience and his work, therefore, is authoritative. His method of treating this subject is original and his division of psychopathic conditions is comprehensive and his treatment is to the point. It is impossible to extensively review a work of this kind because it entails so much. It should be on the desk of everyone interested in the diseases of children and the training of them.

T. H. W.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**Human Infection with Ascaris Mystax.**—BEISELE (*Münch. med. Woch.*, 1911, lviii, 2391) reports a case of human infection with *Ascaris mystax*, the common round worm of the dog and cat. He has found records of only 10 similar cases. The patient was a child, aged two years. During an attack of measles, 15 worms were expelled spontaneously and were found in the bed. Calomel and santonin were administered, and 62 more worms of the same species, together with hundreds of *Oxyuris vermicularis*, were of expelled. It is of interest, as showing the probable source of infection, that two cats and a dog belonging to the family were found to be infected with *Ascaris mystax*; following treatment of the animals, enormous masses of this parasite were obtained.

---

**Rigidity of Certain Back Muscles as a Sign of Pleurisy and the Frequency of Serofibrinous Pleurisies.**—FELIX RAMOND (*Bull. et mém. Soc. méd. d. hôp. de Paris*, 1912, No. 4, 134) finds that if the back of a normal individual in the upright position be examined, in the lumbar region under the twelfth rib on either side of the median line is found a prominence averaging two finger breadths, due to the ileocostal and long dorsal muscles. In patients with pleurisy, this mass contracts reflexly to immobilize the inflamed pleura below, just as abdominal muscles contract in peritonitis, the muscles of the neck and spine in meningitis, or the peri-articular muscles in arthritis. Ramond believes that this phenomenon constitutes a valuable sign in pleurisy. On inspection, the muscles seem prominent. On palpation, they feel harder than normally, and do not relax with change to a lateral position. This

occurs in all pleurisy, appearing before any other sign, persisting after the disappearance of effusion, thus possibly helping to diagnose what has preceded. If it is found bilaterally, it implies bilateral inflammation, especially if combined with dulness. Rigidity of these muscles may, however, occur in cases of intercostal neuralgia, sciatica, pains in the spine, or lordosis. But, on the whole, having eliminated such reflex spinal contractions, the sign in obscure cases draws attention to the possibility of pleural inflammation, and thanks to it, Raymond has been able to diagnose many pleurisy otherwise unappreciable, from which he considers this lesion probably the most frequent intrathoracic inflammation.

---

**Experimental Pneumonia by Intrabronchial Insufflation.**—R. V. LAMAR and S. J. MELTZER (*Jour. Exper. Med.*, 1912, xv, No. 2, 133), in 42 of 48 dogs not selected or prepared in any manner, have produced lobar pneumonia by injecting pneumococci of exalted virulence into the lungs through a catheter or stomach tube by insufflation. Control animals were all negative. Apparently in accordance with the quantity of culture injected the disease was mild, severe, or fatal. Clinically, the disease was characterized by fever and malaise subsiding in a few days without crisis. Pathologically the transition from red to gray hepatization was wanting. Otherwise the anatomical and bacteriological findings agreed with those in man in fibrinous pneumonia. Consolidation occurred quickly. Seven hours after injection nearly complete consolidation of the greater part of one lobe was present. The exudate consisted mainly of well preserved leukocytes, a few red corpuscles, and fibrin. Pneumococci were seen in large numbers. Phagocytes were not numerous. The lymph nodes related to the consolidation were swollen, soft, and moist. By the fourth day resolution was fairly inaugurated, proceeding rapidly but not uniformly. By two weeks the lungs were nearly always normal. In several instances, however, resolution was not complete, and in 2, organization was extensive, though more or less dependent on secondary invasion. In fatal cases one lobe, and sometimes two or three were consolidated. The pleuræ contained large quantities of blood and fibrinopurulent exudate; there was pericarditis and septicemia. This is the first unmistakable experimental evidence of intimate etiological relationship between pneumococcus and lobar pneumonia. It probably is due to the fact that the injected quantity was sufficient to obliterate a group of bronchi, and thus convert their lumina and corresponding alveoli into closed cavities containing pneumococci in the proximity to lung tissue. In other words, Lamar and Meltzer conclude that the question of experimental success does not depend so much on the alteration of the power of resistance of the invaded individual as upon the opportunity offered to organism for intrenchment in invaded territory.

---

**Indiscriminate Drug Taking.**—ALEXANDER LAMBERT (*New York Med. Jour.*, 1912, xcv, No. 7, 313) finds that the danger of forming the habit of continually turning to some drug at the slightest pain in the endeavor to benumb it, instead of finding out what causes it to arise, is in reality very great. For example, many people take headache powders

indiscriminately without a proper knowledge of the underlying cause, which, if removed, will prevent the symptom. Insomnia is another factor which has brought about a widespread use of drugs. Loss of sleep is not injurious; it is the excited condition of mind which produces illness. The danger from drug taking is the disturbance to the health that such an indulgence produces, as well as the diminished mental power following. Rheumatism and gout are terms in popular use which lead to drugging. The public must be educated to the fact that many aches and pains are due to neither, and that the only chance for thorough recovery is through accurate and careful diagnosis, with adequate treatment for the different ailments, commonly grouped under those names. Another prolific source of revenue for the manufacturers of "fake" cures is the large number of people who imagine they are suffering from Bright's disease. It will take many years to break down the enormous amount of ignorance now prevalent concerning the kidneys and their functions. Until this be accomplished unlimited drugging will continue. The crusade against tuberculosis has had one very good result. It has held up to proper condemnation the enormous mass of "fake" cures gathered together and doled out as panaceas. The widespread knowledge as to how these patients should live, and what they should avoid has saved many lives. On the whole, the dangers of indiscriminate drugging may be summed up as follows: The drugs involve great waste since they are used in enormous quantities to no definite purpose; many remedies do harm in that they actually injure and pervert the normal processes of the body.

#### Chemotherapy of Malignant Tumors in Experimental Animals.—

A. v. WASSERMANN, D. v. HANSEMAN, Fr. KEYSER, and M. WASSERMANN (*Berl. klin. Woch.*, 1912, xlix, 4) have made an extensive experimental study of chemotherapy of malignant tumors in mice. At the beginning they decided to discard all substances having a destructive action on neoplasms only when applied locally, for two reasons: (1) The tumor cells often lie in inaccessible places, and (2) more frequently, it is impossible to say where they are. They sought, therefore, only such substances which, when injected into the circulation, are automatically withdrawn by the tumor cells, producing death of the latter, with little or no injury to the normal cells of the body. Immune sera, true cytolytic sera which exhibit a destructive action on tumor cells alone, have not been produced. The one suggestion on which they proceeded was furnished by observations of Gosio who found that sodium selenide and telluride are reduced by living cells. The authors used these salts in experiments to determine whether human cancer cells are more rapidly destroyed in normal sera than in cancerous sera, and found that the reduced elements were deposited in the tumor cells only, especially about the cell nuclei. With this observation they began their investigations on mice suffering with malignant neoplasms. In no case was an animal used for experimentation until its tumor had reached the size of a small cherry; they were careful to avoid ulcerating tumors, in which spontaneous cure is seen at times. Local injections of sodium selenide and telluride, 1 to 1000, caused softening of the tumor which eventually acquired the characteristics of a fluctuating cyst. The cysts were found to contain cell detritus and the two



elements, selenium and tellurium. The mice were cured by this procedure. Now the authors tried intravenous administration, but the toxicity of the preparation was so much greater when given in this way that they were unable to administer enough to have any effect on the tumor. It was therefore necessary to try various compounds of the elements. Since fluorescein and its derivatives are highly diffusible, such compounds were first examined. After experimenting with more than two hundred new compounds, they finally obtained an eosin-selenium preparation which proved to be active. A mouse weighing 15 grams can take 2.5 milligrams of this intravenously. The preparation is very unstable, and is difficult to make as yet. When given to a cancerous mouse, the course of events is as follows: From the first three injections, given on successive days, no result is seen. On the fourth day the tumor feels softer. The fourth injection is given on the fifth day and the tumor at once becomes cystic but still contains firm masses here and there. The fifth injection is made on the seventh day and is followed by a decrease in size of the cyst (absorption). The sixth and last injection, made on the ninth day, leaves what feels like an empty sack. A seventh or eighth injection may be required to produce a complete cure. Animals treated in this way have remained for months without a recurrence. When the tumor is very large or the action of the drug very pronounced, the animals may die, probably from the products absorbed. The larger the tumor, the greater is the danger of death from absorption of toxic substances. If the least particle of tumor tissue remains undestroyed, a recurrence of the tumor will be noted in eight to fourteen days. Since it is mechanically impossible to give more than eight intravenous injections to one mouse, owing to the smallness of the veins and the injury produced in them, and since the drug is inactive when given by mouth or subcutaneously, it has been impossible to determine whether such recurrences may be cured. Four strains of cancer and one of sarcoma were studied. The authors emphasize the fact that their results apply only to the neoplasms of mice and are therefore of theoretic and scientific interest, but that no conclusions with regard to the treatment of cancer and sarcoma in man can be drawn from them. The experiments were controlled very abundantly. Histological examinations of all material were made by v. Hansemann.

---

**Action of Colloidal Selenium A on Cancerous Glands.**—Following the experimental work of WASSERMANN, THIROLOIX, and LAUCIEN (*Bull. et mém. Soc. méd. d. hôp. de Paris*, 1912, 3 s., xxxiii, 197) found by pulverization a product of selenium which they called "Selenium A." It has the physicochemical properties of ordinary selenium, was a colloid of fine suspension, stable, isotonic, and non-toxic to animals. They injected intravenously 4 to 8 c.c. of this once every week for ten weeks into a patient with a painful, ulcerated, non-syphilitic tumor of the tongue accompanied by enlarged, hard submaxillary glands. Each injection was followed by chills, and a temperature of 39° to 40° lasting from one to three days. No other untoward symptoms were noted. After the first injection the glands seemed to decrease in size and become less painful. After the seventh, the submaxillary gland suddenly increased in size, and became fluctuant. Three punctures

obtained nearly 20 c.c. of an aseptic fluid. After the last, the gland had almost completely disappeared. Cytological examination of the centrifuged specimen showed amorphous masses around which were mononuclear cells and rare neutrophilic leukocytes, endothelial-like cells with vacuolated protoplasm and pavement cells. Chemically the liquid gave a positive urobilin test, and showed selenium apparently fixed in the cells. From this case Thiroloix and Laucien believe that selenium can be easily obtained as a colloid suitable for intravenous use, that it only effects very vascular epithelial masses, and that its action is cytolytic. Finally, that though this may be of theoretical important, it is not possible to deduce from this observation a practical application.

---

**Urobilinuria in Pneumonia.**—W. HILDEBRANDT (*Zeit. f. klin. Med.*, 1911, lxxiii, 189) reports a study of urobilinuria in relation to the diagnosis and prognosis of pneumonia and to the interpretation of icterus in the course of pneumonia. He finds that a pneumonia is not complicated by hepatic disease (parenchymatous hepatitis, chronic passive congestion, or bile stasis) when the urobilin curve is only slightly above the normal at the beginning of the disease, high during crisis, with a rapid fall coincident with the termination of resolution. Chronic passive congestion is dependant entirely upon the condition of the heart. Bile stasis, causing the pleiochromic icterus, may be confused with icterus resulting from a parenchymatous hepatitis. Pleiochromic icterus, which is rarely uncomplicated by hepatitis of some degree, is concomitant with resolution, and is attributable to the excess of blood pigment carried to the liver from the resolving pulmonary exudate. Parenchymatous hepatitis, on the other hand, appears on the urobilin curve at a time when signs of resolution are lacking. For prognosis, the recognition of a parenchymatous hepatitis at the beginning of a pneumonia is of great importance; it indicates a severe general infection. The continuation of an increased urobilinuria after the resolution is completed is indicative of a parenchymatous hepatitis which may clear up on prolonged treatment in bed or, rarely, may become chronic. In pneumonia, then, Hildebrandt believes that the beginning and end of resolution may be determined with considerable accuracy by following the urobilin curve. In obscure cases (central pneumonia) the urobilin curve may be of great aid. It is important, of course, that conclusions be based on daily observations, not on isolated findings.

---

**The Rectal Administration of Salvarsan.**—S. L. BARGROW (*Berl. klin. Woch.*, 1912, xlix, 108) has used salvarsan in suppositories in cases where intravenous or intramuscular administration seemed inadvisable. The suppository is made to contain 0.1 to 0.2 gram salvarsan and 0.01 gram novocain. A suppository is given at two to three-day intervals till the desired amount of the drug has been given. The bowels should not move till ten to fifteen hours have elapsed after giving the suppository. The effect of the drug is manifest in three to four days and there is practically no reaction, either local or general.

## SURGERY

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**The Surgical Treatment of Hypertrophy of the Thymus.**—OLIVIER (*Archiv. gén. d. Chir.*, 1912, vi, 138) rejects radiotherapy in these cases. The only preventive and curative treatment to be considered is the surgical. Since 1896, three different operations have been practised; exothymopexy, resection of the manubrium sterni, and thymectomy. Exothymopexy consists in exposing the thymus through a longitudinal incision above the sternum, opening the mediastinal space in its upper part, catching the gland and its capsule with a forceps, and after drawing it out as far as possible, fixing it by sutures to the suprasternal fascia. It is not a satisfactory operation, and is excluded. Resection of the manubrium sterni is done to increase the superior orifice of the thorax and thus to relieve compression, but as a means of relief of the condition, is rejected absolutely by Olivier. Thymectomy is the only rational treatment, and may be partial or total, subcapsular or extracapsular. The operation of choice is what Olivier calls the subcapsular, subtotal operation, all of the gland that can be seen being removed. General anesthesia with chloroform is to be preferred, but it is to be administered with much caution, and the inhalation is to be suspended immediately if the amplitude of the pulse or respiration begins to diminish. Two points are insisted on in the preparation of the infant. The dressing must be thoroughly dry and the field of operation is not to be washed immediately before the operation. Otherwise the water will cause the epidermic cells to swell and the tincture of iodine will then not penetrate. In the second place, the excess of the tincture of iodine should be removed with alcohol to avoid vesication, the infant's skin being very sensitive. The child should be on its back with a pillow under the shoulders, to make the field of operation prominent. The incision should be longitudinal and median, from 3 to 5 cm. long, ending below from 1 to 5 cm. below the upper border of the sternum. The cutting and avoiding of the various structures are described with much detail. When the capsule of the thymus is exposed and carefully opened, one lobe of the gland is then easily separated from the surrounding structures and brought upward from its location behind the upper end of the sternum. A catgut ligature is applied to its base and the lobe removed. The other lobe is then removed in the same way. The cavity is then closed by suturing the subhyoid muscles in the

median line and approximating the sternomastoid muscles. The skin is sutured without drainage. Of 42 thymectomies collected, there were 27 cures and 15 deaths, or a mortality of about 35 per cent. Thymectomy in itself, without drainage, tracheotomy, nor removal of infected nodes, has no operative mortality.

**The Employment of Iodine Disinfection in the Opened Gastrointestinal Tract.**—PAYR (*Zentralbl. f. Chir.*, 1912, xxxix, 386) reports on the results which he has obtained with Fritzsche's method of using iodine in these operations. He says that for three years, in all cases in which he opened the gastrointestinal tract, he has applied tincture of iodine once or twice to the mucous surface, although he has during this time somewhat altered the method. The necessity for frequent performance of transverse resection of the stomach for ulcer at the lesser curvature or on the posterior wall, led him to use tincture of iodine for disinfection of the mucous membrane. It is often difficult to close the short cardiac portion of the stomach with the aid of the usual forceps. He has frequently completed the axial lines of sutures of the cardiac and pyloric ends without a sufficient closure of the former by the forceps, many times employing a strip of gauze to close it. In these cases he has coated the mucous surface of the broad gaping stomach with tincture of iodine. He has used it also in gastroenterostomies, enteroanastomies, and all intestinal resections. When there is a thick layer of mucus on the gastric mucosa, it is wiped dry, and the iodine applied vigorously. In the large intestine the contents are also carefully wiped away with pads before applying the iodine. The color of the iodine disappears gradually from the gastric mucosa, rather more quickly than from that of the intestinal mucosa. It might be supposed that the iodine would produce marked irritation of the wound margins of the stomach or intestine, and that this would interfere with the rapid progress of the healing process. Payr has not observed any bad results (increase of the complications from adhesions, intoxication), and in cases in which the abdomen was opened later by operation, or autopsy, the field of operation was faultless.

**Extirpation of the Gasserian Ganglion under Local Anesthesia.**—KRAUSE (*Zentralbl. f. Chir.*, 1912, xxxix, 385) reports that in January of this year, he removed the Gasserian ganglion by Braun's method of local anesthesia with novokain-adrenalin. The patient was a woman, aged seventy-two years, suffering from a severe arteriosclerosis and an uncompensated heart-valve lesion. She had had all the peripheral branches of the trigeminus resected, and had received alcohol injections without relief. Three quarters of an hour before the beginning of the operation by Krause, a subcutaneous injection of scopolamine and pantopon was given. Then at the anterior and posterior ends of the zygoma, 5 c.cm. of the novokain solution was injected subcutaneously, and the same quantity subperiosteally at the upper and lower borders of the bone. From a point at the middle of the upper border of the zygoma, the whole region of the temporal osteoplastic flap was injected subcutaneously and subperiosteally with about 5 c.cm. of the solution. Further there was injected outward from the mouth in all directions, to the height of the temporal process of the mandible, two syringefuls, one containing 5 and the other 10 c.cm. This rendered the soft tissues

and bone painless in the region of the temporal fossa, as well as the third branch of the trigeminus. Because of the addition of the adrenalin to the solution injected, the bleeding was very slight. The beginning of the operation, including the separation of the dura from the inner surface of the temporal bone and the cutting of the bone, were carried out without any evidence of pain. The patient complained slightly when the dura was being separated from the base of the skull with small pads. As soon as the middle meningeal artery was exposed, 2 c.cm of the solution were injected forward, backward and medialward, into the dura and as far as possible into the parenchyma of the ganglion. Thus the dura, the ganglion and the second and third divisions of the nerve were invaded. The exposure of these structures was carried out without any considerable pain. When the second and third divisions of the nerve and the ganglion were being separated, the patient again complained slightly and clenched her hands. In the empty Meckel's space, could be seen the unwounded abducens nerve. The pulse scarcely changed its character during the operation. When the patient recovered from the effects of the scopolamine, some hours later, she stated that she had no recollection of the operation. The wound healing, was without disturbance, and on the fourth day the patient got out of bed. Krause regards the method of anesthesia as an important advance in operative surgery, since it permits us to dispose of general anesthesia in cases with such severe heart affections as in this patient.

---

**The Experimental Production of Basedow's Disease.**—BARACH (*Zentralbl. f. Chir.*, 1912, xxxix, 316) says that Eugene Bircher's interesting report on the experimental production of this disease by implanting pieces of the thymus in the omentum of dogs, leads him to report again in a preliminary way, he having already reported on the same subject in this journal (1911, xxxviii, No. 35). The material he employed was from human goitres, which were mostly of the parenchymatous variety, rarely of the colloid. The goitre tissue was ground up fine a few hours after operation and injected into the animals through a syringe, with a large needle, subcutaneously or under the peritoneum. The subcutaneous injections did not produce noteworthy results in the desired direction. The intraperitoneal injections, however, carried out in a series of dogs as well as rabbits and rats, produced the typical Basedow's disease. The dogs showed much excitement, a nervous condition, and much wasting. There was also marked falling out of the hair and diarrhea. There were further, tachycardia, glycosuria, lymphocytosis, and in some, marked exophthalmos was observed. In one of the dogs in consequence of the exophthalmos, there developed a corneal ulcer. The experiments were not always positively successful, but were most successful in young animals and in females. The amount injected was from 5 to 20 c.cm., and was usually repeated at intervals of about eight days. The exophthalmos developed in from twelve to fourteen days. Klose employed for the same purpose the fluid pressed from ordinary goitres and exophthalmic goitres, but succeeded only with the fluid from the latter, in producing symptoms of a transitory character, by injecting it intravenously. Exophthalmos occurred only in two cases and only for two days. This would seem to show that the active principle in Basedow's disease, was present only in small amount

or not at all in the fluid pressed out. From Bircher's and Barach's experiments, it is shown that the typical picture of Basedow's disease can be produced from material other than that arising from patients suffering from the disease.

---

**The Use of Tincture of Iodine in the Treatment of Surgical Tuberculosis.**—WOLFF (*Zentralbl. f. Chir.*, 1912, xxxix, 347) following Francke has employed this method in two cases and recommends it strongly. The first case was that of a soldier with tuberculous involvement of the right acromioclavicular articulation. A large abscess covered the shoulder region from the middle of the clavicle to the middle of the deltoid. The skin over it was somewhat bluish and threatened perforation. The x-rays showed a sequestrum in the region of the joint affected. The abscess wall was freely exposed by turning back a flap of skin, and was cleaned away. Caseous pus, however, came into contact with the surrounding healthy tissues. After the hemorrhage was controlled by compresses, the whole wound was covered with a 10 per cent. tincture of iodine. The wound was then closed by sutures, a gauze drain being left in for a few days to carry off the wound secretions. Complete healing occurred seventeen days after the operation. In just one month, the patient went back to service as a soldier, and since then has performed all his duties without difficulty. In the second case, also a soldier, there was a well-advanced tuberculous adenitis on the left side of the neck, the abscess being about to open. A clean removal of the abscess membrane was impossible because of the callous invasion around it. The tuberculous granulations were removed with a sharp curette and all pockets and grooves of the wound washed out with the 10 per cent. tincture of iodine. The wound was closed with the exception of a small opening for drainage, the drain being removed in four days. Complete healing occurred in three and one-half weeks, and the patient returned to the service five weeks after the operation. The tincture of iodine appears to be an excellent means for improving the course of healing after operation for tuberculosis of the bone and soft tissues.

---

**Osteomyelitis of the Long Bones.**—HOMANS (*Annals of Surgery*, 1912, lv, 375) says that osteomyelitis of the long bones in children originates in the ends of the diaphyses—rarely as periostitis. It principally attacks the weight-bearing bones. The early or primary operation demands the removal of bone for drainage only. The infected medulla should be fully uncovered without doing unnecessary damage to the periosteum or endosteum. Considering the power of regeneration of periosteum plus endosteum, early complete resection of a shaft is not advisable; therefore total resection later should be reserved for cases of total necrosis. The Röntgen rays cannot be depended on for diagnosis in the very early stages, but is invaluable for following the course of the disease.

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

**The Treatment of Lobar Pneumonia.**—LÖWENSTEIN (*Med. Klinik.*, 1912, viii, 145) compares the results obtained since the replacement of digitalis preparations as cardiac tonics in pneumonia by camphor and caffeine. He reports 184 cases treated with the aid of camphor and caffeine stimulation. The mortality in these cases was 10.4 per cent., as compared to a mortality percentage of 17.7 by the former method of treatment. In the series of cases treated by Löwenstein, he notes that most of the fatal cases were in the old people where the pneumonia was a terminal infection, and in alcoholics. Löwenstein believes that both camphor and caffeine are far superior to digitalis as cardiac tonics in pneumonia.

**Carbohydrate Cures in Diabetes.**—STRAUSS (*Deutsch. med. Woch.*, 1912, xxxviii, 441) gives a general summary of the treatment of diabetes by different dietetic measures, especially those dependent upon periods of limitation of the diet to certain specific substances. With reference to "milk cures," he states that they are of definite value in certain cases of diabetes, but tolerance of the milk must be determined for the individual case. The various carbohydrate cures owe their beneficial effect to the absence of animal protein and their low caloric value and hence they are practically starvation cures. Another factor is that the starch is very slowly absorbed, and this slowness in assimilation prevents a marked increase in the glycosuria. It has been established that when carbohydrates are given in small amounts distributed throughout the day that they do not produce as marked glycosuria as when taken in large quantities. Consequently an essential feature of the carbohydrate cures is to give the carbohydrate in small repeated amounts. Experience with the oatmeal cure has been fuller than with other carbohydrate cures, but Strauss does not believe that it is superior. Lately a number of observers have reported equally good results with the wheat meal treatment of diabetes. The "potato cure" sometimes will be successful when other methods fail. Strauss adds that it is most important not to give a mixture of different starches, but to adhere definitely to a single form of carbohydrate, for better results are obtained when the carbohydrate is given in a pure form than when combined. The carbohydrate days cannot be kept up for long periods, for they furnish less than the required amount of protein. Attempts to make up the required protein by the substitution of various vegetable proteins for animal protein thus far have not been successful. Strauss has had excellent results by the interposition of a fluid day in the treatment of severe diabetes. The patient is allowed on this day nothing but tea, coffee,

bouillon, mineral waters, wine or brandy, and sometimes oranges. The author believes that his experiments and clinical observations indicate that inulin is better tolerated in diabetes than any other form of starch. The addition of inulin to the diet does not increase the glycosuria. He found that comparatively small amounts were recovered from the feces after its administration, and therefore he believes that it is largely assimilated. Strauss suggests the use of inulin, especially in severe cases of diabetes with acidosis by the method of a course of several "inulin days." As inulin itself is very expensive and difficult to obtain, vegetables rich in inulin should be ordered, such as artichokes, salsify, dahlia tubers, etc.

---

**The Treatment of Pneumonia with Camphorated Oil.**—WACHTER (*Med. Klinik.*, 1912, viii, 403) confirms Löwenstein's observations regarding the efficacy of the treatment of lobar pneumonia by camphor. Wachter has been giving his pneumonia patients injections of from 3 to 5 c.c. of camphorated oil once or twice a day as a routine measure. He believes that it has a direct sedative action upon the brain; the mental distress subsided, and even the delirious patients became quiet in the 30 cases treated by Wachter. He is also convinced that it is very effectual as a heart stimulant, and in addition it seems to have a beneficial effect upon the dyspnea.

---

**The Value of Inulin as a Foodstuff.**—LEWIS (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1176) relates his experiments that were undertaken to determine the value of inulin as a substitute for starch in the diet. Inulin occurs in the roots of many plants particularly in the artichoke, elecampane, dandelion, dahlia, and other similar plants. The feeding of these vegetables has been advocated by many as a substitute for starch in the dietary of diabetes. This recommendation is largely based upon the fact that the administration of these vegetables causes no increase in the amount of sugar in the urine. Strauss reports the feeding of pure inulin with much benefit in two cases of diabetes. Pure inulin is very expensive and difficult to obtain, and hence its use is not practical. Certain observers have claimed that inulin produces no increase in the sugar excretion, because it is not absorbed. Neubauer found in a case of levulosuria no increased levulose content of the urine after feeding 80 grams of inulin. If inulin were converted in the body to levulose, then a large increase in the levulose content of the urine was to be expected. No inulin was found in the feces, but the patient observed a strong gas formation in the intestine during the period following the meal, indicating bacterial decomposition of the inulin. The colon bacillus and other intestinal bacteria decompose inulin without the production of sugar. Lewis says that the facts he obtained in his experiments seemed to indicate that any utilization of inulin can occur only after hydrolysis by the gastric juice. The extent of this hydrolysis must vary with conditions in the stomach. If the diet is of such a character that it leaves the stomach soon, the action of the acid gastric juice is checked by the intestinal reaction before the inversion of inulin can proceed far. The acidity of the gastric contents also must influence the rate of inversion. The character of the diet and individual peculiarities both play a role here. Hence the percentage



utilization of inulin for any individual must vary and cannot be determined except by experiment. Any inulin which leaves the stomach unchanged is liable to escape utilization and undergo bacterial decomposition in the intestine, a decomposition which results in no formation of carbohydrates. Any inulin which escapes this bacterial action is probably eliminated unchanged in the feces. In view of these facts, as well as the inability to administer more than comparatively small quantities, the value of inulin as a significant source of energy in human dietaries must be questioned.

---

**The Vaccine Treatment of Croupous Pneumonia.**—RAW (*Lancet*, 1912, clxxxi, 646) treated 207 cases of lobar pneumonia by a stock pneumococcus vaccine. The total mortality in the cases treated was equivalent to 16 per cent. Raw notes as a striking feature, that he attributes to the vaccine treatment, the total absence of empyema in this series of cases and the development of but few other complications. However, he saw no effect in hastening the appearance of the crisis or in shortening the duration of the disease. Raw says he is convinced that we have in pneumococcus vaccine a valuable aid in the treatment of pneumonia, and although not a specific remedy, it ought always to be used in cases of a virulent type.

---

**The Results Obtained by Combined Sanatorium and Tuberculin Treatment of Pulmonary Tuberculosis.**—RADCLIFFE (*Lancet*, 1912, clxxxii, 791) summarizes the results obtained by sanatorium treatment of tuberculosis alone as compared with the combined sanatorium and tuberculin treatment as follows: 1. As the immediate result of sanatorium treatment alone we can expect only from 20 to 25 per cent. of all patients to lose the bacilli from their sputum. 2. When the use of tuberculin is combined with sanatorium treatment at least 50 per cent. of all cases will lose their bacilli. 3. The earlier the cases come under treatment the better are the results. This is strikingly shown in the tables in which the cases are considered in groups according to the stage of the disease. 4. The immediate results are so strongly in favor of the use of tuberculin that it is difficult to understand the opposition to its employment, both in treatment and diagnosis.

---

**Salvarsan Fever.**—HECHT (*Med. Klinik.*, 1912, viii, 401) gives the following factors as causes for untoward symptoms that may develop after salvarsan injections: (1) The use of unclean salt solution in the preparation of the salvarsan for injections. (2) The setting free of endotoxins from the spirochete destroyed by the salvarsan. (3) In a few cases a specific toxic action of the salvarsan itself. Hecht believes that the first cause explains the great majority of the febrile reactions occurring after salvarsan injections. He says that most of the untoward symptoms may be avoided by using only freshly distilled water in the preparation of the salt solution.

---

**Acute Articular Rheumatism Treated by the Rectal Administration of Sodium Salicylate.**—HEYN (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1013) advocates the rectal administration of sodium salicylate for the treatment of acute articular rheumatism. The rectal administration

is to be preceded by a cleansing enema of plain water and two to four drams of sodium salicylate are then incorporated in an enema of six ounces of starch water and from five to ten drops of tincture of opium. This enema is, as a rule, readily retained. Heyn says that this procedure has been resorted to in 22 cases, 5 of which were not typical instances of acute rheumatic fever, but the therapeutic test was nevertheless applied. No unfortunate results happened in any instance, though frequently the dosage reached 240 grains daily. One case only was intolerant to the remedy, owing to a previous irritability of the rectum. All typical cases were more or less benefited, and these results obtained with the rectal administration of sodium salicylate should warrant its use, not only in cases in which the stomach is intolerant, but, where possible, as a routine measure.

---

**The Treatment of Chronic Cardiac Insufficiency by Intravenous Injections of Strophanthin.**—FRAENKEL (*Münch. med. Woch.*, 1912, lix, 289, 371) advocates the intravenous injection of strophanthin in certain cases of cardiac insufficiency, especially when digitalis treatment fails to benefit. A sovereign indication for this method of treatment is pulmonary congestion due to acute dilatation of the heart. A single injection of strophanthin is often sufficient to relieve the patient of distressing symptoms in some cases, and subsequently the improvement may be maintained by digitalis preparations given by mouth. Fraenkel uses Strophanthin Boehringer, giving as the initial dose 0.5 milligram that may be repeated twenty-four hours by a second dose. His usual practice is to repeat the dose only when the favorable effect from the previous dose is no longer apparent. He relates a case in detail of a woman with a valvular lesion and chronic myocarditis who was made very comfortable by small repeated injections of strophanthin. This patient was not able to take digitalis by mouth, but there were no untoward symptoms from the strophanthin injections, and during the course of a year and a half she received 85 injections. At the end of the treatment the ascites, that had previously necessitated frequent tapping, had entirely disappeared, and the formerly congested and painful liver had become much smaller. The patient was able to walk comfortably on level ground, and no longer required morphine at night to make her sleep.

---

## PEDIATRICS

---

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,  
OF PHILADELPHIA.

---

**The Effect of Summer Heat on Infants and Children.**—EUGEN SCHLESINGER (*Deutsch. med. Woch.*, 1912, xxxviii, 558), in a discussion of the almost unprecedented mortality among infants during the preceding summer in the larger German cities, shows that housing and

environment modify greatly the general effect of summer heat on infant mortality. From the mortality curves of three localities having the same climatic conditions, and in which the milk supply and general care of infants were practically identical, it is seen that the infant mortality of one of these localities rises higher to a marked degree during July and August than that of the other two places. In the first locality the houses were packed one against the other, the whole district congested, with no open spaces around the dwellings. The fact that the rooms and houses did not cool off during nightfall, that air currents could not vary the temperature, and that practically a heat stagnation existed accounts for the high mortality in this district. The other districts were less congested and the houses spared to some extent admitting air, and the heat was more intermittent. Long sustained, high, room temperature plus humidity and air stagnation are therefore important factors which modify the general effect of summer heat on infants. Among other effects of summer heat were found frequent cases of "heat stroke" in children similar to that found in adults. The symptoms comprised coma and convulsions, increased temperature and continued unconsciousness ending in death within a few days. These cases occurred among the apparently well nourished children fed on some prepared or condensed baby food. The general effect of summer heat is to lower resistance and vitality in the healthy child, causing at times elevation of temperature; to retard the improvement in bottle fed babies; to reduce tolerance; to nourishment and to augment the severity of gastro-intestinal diseases. Changes in diet and general hygiene are of vast importance during summer heat. Food should be less concentrated and even reduced in bulk. A liberal quantity of liquid should be given. Frequent cool and tepid sponging and light clothing both day and night are imperative, especially in congested districts. In older children, aged from six to ten years, it was found that 30 per cent. in 260 lost appreciably in weight from May to August. Schlesinger attributed this especially to the effect of summer heat in school-rooms, with their attendant air stagnation and humidity. After seven weeks' vacation, although the heat remained intense, the children had regained the weight lost and many had added to their former weight.

---

**Lordotic Albuminuria.**—FRANZ HAMBURGER (*Wien. klin. Woch.*, 1912, xxv, 262) agrees with Jehles' discovery that in many children an albuminuria can be caused or increased by a lordosis. There is no doubt that most of the so-called albuminuria of puberty can be traced back to a lordosis in the lumbar vertebræ and that a lordotic albuminuria depends upon a blood stasis in the kidneys: another theory is that both kinds of albuminuria are influenced by nervous and vasomotor changes. There is no doubt that most individuals with lordotic albuminuria have vasomotor disturbances and that the large number of cases occurring in children, aged from seven to fifteen years, is due to the fact that during the period of puberty the vasomotor system is especially unstable and irritable. Individuals with angioneurotic or "vasomotor" tendencies will react more with an albuminuria in lordosis than will normal, healthy individuals. The same person under the same conditions may show albuminuria at one time, and at another show only a slight amount or none at all. This is probably due to

changes in the degree of lordosis and is purely mechanical. However, it is also due at times to existing vasomotor conditions which modify the mechanical factor.

---

**Syphilitic Affections of Bones in Childhood.**—DUNCAN C. L. FITZWILLIAMS (*Brit. Jour. Child. Dis.*, 1912, ix, 97) points out that the terms "congenital" and "hereditary" are really obsolete as applied to syphilis, since all syphilis is "acquired," either before, during, or after birth. The only difference lies in the reaction produced in young and growing tissues as contrasted with that found in well formed tissues. In the adult form it can be roughly graded into its three stages. In infancy and childhood, owing to a lesser resistance, the process is unchecked. A stage of incubation is followed by a jumble of symptoms in which the macular rash and the gumma may be seen at the same time and the condyloma may show the true nature of a bone lesion. In childhood syphilis shows a predilection for the shaft of bones ignoring the epiphysis almost entirely. In joints the condition begins in the synovial membrane and not the bony parts. The condition known as syphilitic epiphysitis is really a perichondritis affecting the whole length of the bone. The humerus, radius, and ulna are more frequently affected than the femur, while the tibia and fibula are rarely attacked. Syphilitic perichondritis practically always occurs in children below six months. Rashes, snuffles, condylomata and a family history of miscarriages are helps in diagnosis. Syphilitic dactylitis is rare, causes no pain and occurs usually after the third year of life. Periostitis is the commonest manifestation in bones and the local form occurs about the fifth or sixth years, is usually started by some injury, and affects the upper part of the tibia and the ulna for that reason. Generalized periostitis involves the whole shaft of the bone, seldom encroaching on the epiphysis, and usually appears later in life than the localized form. In the tibia the forward bend in the bone is marked in the upper part and occurs after the child has learned to walk. In rickets the forward bend is low down in the bone and develops before the child has learned to walk. In syphilitic osteomyelitis the whole thickness of bone is attacked and replaced more or less completely with gummatous tissue. The treatment followed out by Fitzwilliams with much success consists in immobilization of the affected limb, liq. hyd. perchlor.,  $\text{Mv}$  in cod-liver oil by mouth and occasionally mercury ointment and lanoline by inunction. He has not employed salvarsan in any of his cases.

---

## OBSTETRICS

---

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

---

**Sepsis in the Newborn Originating in Bednar's Aphthæ.**—LINDENMEIER (*Zentralbl. f. Gynäk.*, 1911 No. 50,) reports the case of an infant

born in normal labor, at full term, of slightly more than average development. At birth the mouth was not wiped or washed out, and the child was nursed by the mother. At first it gained in weight, and then commenced to lose, with frequent vomiting. Six days after birth the child had an excessive seropurulent discharge from the nose. On inspecting the mouth a reddened area covered with a yellowish secretion was found, and bacteriological cultures were made from this region. Diphtheria was excluded, and the child's temperature was normal. The condition increased until the child was unable to nurse or drink, and was fed by the introduction of a catheter into the stomach. The child frequently vomited a thick, yellowish membrane. Neurotic particles were finally discharged, and the mouth and gums bled freely. The child died cyanotic. On section extensive membranous inflammation of the pharynx and larynx were present. There was a neurotic condition of the mucous membrane of the esophagus and stomach, with beginning bronchopneumonia. The lungs were emphysematous, the intestine empty. The liver and spleen were swollen, and from the neurotic tissue hemolytic streptococci were isolated. The mother's puerperal period was normal, although hemolytic streptococci were obtained by culture from the lochial discharge. The second case was that of an infant born in normal labor, the umbilical cord wound once around the neck, causing slight asphyxia. The mouth of the child was cleansed with sterile linen. The child was slightly premature. It nursed the mother normally, but on the sixth day began to have a discharge from the nose. The Wassermann reaction was negative for mother and child. The child died with the symptoms reported in the previous case, and autopsy showed evidence of extensive septic absorption. The mother had mastitis in the right breast, caused by hemolytic streptococci, which were also obtained from the lochial discharge. She evidently made a good recovery. The third case was that of an infant born in transverse position, with lateral placenta prævia. Version and extraction were performed, the child being slightly asphyxiated, but readily revived. The mouth was washed out at the time. The child was above the average in development, but did not nurse well, and speedily lost weight. Seven days after birth a nasal discharge began containing streptococci. Swelling of the mouth and gums developed, with a yellowish exudate, followed by rapid failure of strength, and death. Autopsy showed hemorrhagic necrosis in the mucous membrane of the mouth, esophagus, and stomach. The infective agent was the hemolytic streptococcus. This was found in the mother's discharge, although she made a good recovery, with but one very slight elevation of temperature. These cases are diagnosticated as Bednar's aphthæ, complicated by a streptococcus infection.

---

**The Disinfection of the Hands by Acetone Alcohol.**—HABERLE (*Zeits. f. Geburts. u. Gynäk.*, 1911 Band lxi, Heft 2,) reports the results from his experiments in Hofmeier's clinic at Würzburg, with disinfecting the hands by acetone alcohol. In 25 experiments the hands were rendered practically sterile, and so remained during and after the operations performed. These experiments were made upon persons who were not skilled surgeons, and assistants who were not proficient in minute technique. The hands in many operations became

somewhat sodden with moisture, and the virtue of the acetone alcohol method lies in its efficient action upon the upper layers of the skin. There seemed to be no practical difference in the action of a 20, 30, or 50 per cent. mixture of acetone and alcohol. As acetone is more costly than alcohol, this might become for extensive use a matter of importance. It is probable, however, that the higher percentage of acetone increases the action of the alcohol. In experimenting, the hands were artificially infected with staphylococci and allowed to dry completely in atmosphere. The use of 30 per cent. acetone alcohol produces efficient disinfection. As regards the permanency of its action, the hands previously disinfected with acetone alcohol were examined after operations lasting thirty minutes, when perspiration forming in the hands had moistened the skin. It was found that the method was efficient, and that even when germs were present they were in the vegetating form and not actively virulent. It is believed that if possible the hands should be brushed for three minutes with hot water and soap, followed by the application of acetone alcohol as soon as possible. Where but a short time can be taken in this washing, the acetone alcohol should be used a longer time, if possible. To test the efficiency of the method, the hands were disinfected with acetone alcohol, and then inserted into very large sterile rubber gloves, containing warm sterile water, and the hands thoroughly soaked and rubbed in these gloves. The gloves were gauntlets extending to the elbow, and the temperature of the water was kept as high as it could be borne. After thirty minutes the gloves were carefully removed and the water examined for bacteria. A portion of them were found sterile; others had a few bacteria, non-pathogenic; and others had a small number of bacteria. His experience shows that this method efficiently disinfects the superficial layers of the skin of the hand for at least thirty minutes. Operators can readily repeat the disinfection at these intervals during a prolonged operation. In this connection recent experiments in von Herff's clinic at Basle, made by Hüssy (*Zeits. f. Geburts. u. Gynäk.*, Band lxxix, Heft 2, 1911) are of interest. He has experimented with an alcoholic preparation of soap, which he described as a 10 per cent. tetra-ethylen soap. It is non-irritating and efficient in disinfecting the skin. It may be used by rubbing the parts with sterile cotton pledgets and the suds washed away with sterile water, or 96 per cent. alcohol, with pieces of sterile flannel. After mechanical cleansing of the nails a similar process may be employed upon the hands.

---

**The Wassermann Reaction, with or without Treatment by Salvarsan.**—HERMANN and STERN (*Zeit. f. Geburts. u. Gynäk.*, 1911, Band lxxix, Heft 2,) have investigated the importance of the Wassermann reaction in the diagnosis of syphilis complicating pregnancy. In 80 cases of pregnant women the reaction was negative in 61, and positive in 19. Among these 19 a positive diagnosis of syphilis could be made from skin lesions in 8; in 4 the history was very significant of syphilis from the birth of a macerated child, and from other circumstances. In 2 syphilis was evidently present, from the repeated birth of macerated children; in 3 the Wassermann reaction was positive, although the mother showed no signs; but in 2 cases the children were syphilitic,

and in 1 case the child and husband also; in 2 cases in which a positive reaction was obtained, one could find no other evidence of syphilis. In 4 cases of eclampsia—3 severe and 1 mild—the reaction was negative. When the 61 patients who gave a negative reaction were examined, 56 were found to be absolutely free from any sign or symptom of syphilis; 5 cases were suspicious, 3 of them had given birth to macerated children, and 2 had received treatment for syphilis. In 22 cases of abortion the reaction was positive in 3 patients. As regards the nursing of the children by the mother, where the reaction is positive in both mother and child, there can be no objection to the child nursing. Where the reaction differs in the two, the child must be artificially fed. Four cases were examined who had received treatment with salvarsan. The first had a characteristic eruption during pregnancy, and the Wassermann reaction was positive. After treatment by salvarsan the patient went to term and was delivered spontaneously of a full term living child. Shortly after delivery the Wassermann reaction was positive in both mother and child, and four weeks later positive in one and negative in the other. The second case had acquired syphilis three years previously and had received treatment. She gave birth to a living child, and the reaction was negative in both mother and child. The third patient had received the salvarsan a few weeks before the termination of pregnancy. During the puerperal period the mother gave a positive, the child a negative reaction. In the fourth case the mother just before labor received salvarsan, and after labor both mother and child gave a positive reaction.

---

**Repeated Pregnancy after Plastic Operations upon the Tube.**—WESENBERG (*Zentralbl. f. Gynäk.*, 1911, No. 51,) reports the case of a patient from whom he had removed the left pregnant tube, and had performed a plastic operation upon the right tube, which was adherent, to render it patulous. A year afterward pregnancy occurred in this tube. The patient had been married ten years without pregnancy, and was delayed considerably over one period. Pain in the abdomen developed, with characteristic symptoms of tubal gestation, and upon operation removal of the left tube and ovary was performed. The right tube was thickened, and its fimbriated extremity completely closed. An opening was made into this extremity, and the mucous membranes carefully stitched with fine catgut to the serous covering of the tube. She returned a year afterward with symptoms of abdominal disturbance, and upon operation the right tube was found pregnant, and the tube and ovary removed. Microscopic examination proved the existence of the tubal pregnancy.

GLITSCH (*Arch. f. Gynäk.*, Band lx, 1911) in a paper on the etiology of tubal pregnancy reports a similar case. He had removed a blighted ovum from the left tube and performed a plastic operation upon both tubes to render them patent. A year and a half afterward the patient had a molar pregnancy, and two and a half years later a uterine abortion complicated by tubal pregnancy on the left side, which came to spontaneous recovery after abdominal operation.

## GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

**Vaginal Route in Bladder Operations.**—MICHEAL (*Folia Urologica*, 1912, vi, 575) draws attention to the fact that, in recent years, owing to the active contest between supporters of the endoscopic and suprapubic methods of attacking the bladder, the easy route by way of the vagina has largely been overlooked. He believes, however, that there are many cases in which it possesses decided advantages on account of its *simplicity and freedom from danger, combined with thoroughness* and the possibility of obtaining access to practically the entire interior of the bladder. In cases of multiple papillomas, for instance, the vaginal incision, properly carried out, gives as good an opportunity for thorough removal as does the *sectio alta*, and is a much less serious operation; the endoscopic methods, which are frequently applied to the treatment of these cases, are always accompanied by a certain amount of danger of recurrence, owing to malignant changes having taken place in the basal portion of the tumors. Micheal believes, moreover, that a tearing off, crushing, or cauterization piecemeal, in many sittings, as is frequently necessary in treating multiple growths by endovesical methods, must certainly furnish a greater stimulus to proliferation than thorough, direct extirpation in one sitting. With regard to technique, Micheal has found the simple, longitudinal incision in the midline, beginning about 2 cm. in front of the cervix, sufficient in uncomplicated cases of stones, foreign bodies, etc., which for some reason could not be removed through the cystoscope. In making this incision, care must be taken to keep exactly in the midline, so as not to injure the ureters, and the incision must not be extended far enough forward to involve the sphincter of the urethra. In cases, however, where it is necessary to obtain access to all parts of the inner surface of the bladder, as in multiple papillomas, the simple longitudinal incision does not suffice. The T-shaped incision of Simon is open to various objections; it presents some risk of injuring the ureters, it does not expose the ureteral orifices to view, and it leaves a two-pointed wound, which is difficult to close in a satisfactory manner. Micheal has found the most satisfactory exposure to be afforded by a transverse incision through the trigonum itself, this being increased if necessary to an arched incision by extending it at each end upward and outward for a distance of 1 to 2 cm. The tongue-shaped flap, including the trigonum vesicæ, thus formed, can now be turned under, and the interior of the bladder fully exposed. In order to avoid injury to the ureters it is well to have the bladder rather fully distended (150–200 c.c. of fluid), and to carry the incision down to the mucosa with a sharp knife before the bladder is opened. A previous cystoscopy will show in each case whether a long or short trigonum is present. In some cases of narrow vagina a slight



perineal incision is necessary to afford access to the anterior wall. In uncomplicated cases the patient can be out of bed the following day; in infected cases there is practically no danger of infection of the vesicovaginal septum, as drainage can be secured by the use of a permanent catheter. In cases where, on account of hemorrhage, or of the impossibility of freeing the bladder walls from secretions, ureteral catheterization through the cystoscope has failed, this method of colpocystotomy may be used for direct catheterization of the ureters. After opening the bladder, and inserting the catheters into the ureteral orifices, the other ends are passed out through the urethra, and the bladder wound immediately closed.

---

**Ovarian Tuberculosis.**—In studying a rather small series of cases of genital tuberculosis, COHN (*Arch. f. Gyn.*, 1912, xcvi, 497) found the ovary involved in two-thirds of the cases, in all of which, however, there was marked tubal and perioöphoritic involvement. That the ovary is not involved more frequently he believes to be due to a considerable thickening of the albuginea which he found in all cases. This is evidently a reaction to the perioöphoritic tuberculous process, and offers a distinct resistance to invasion of the ovary itself. Opportunity for such invasion is afforded, however, by openings on the surface of the ovary, resulting from follicle rupture; in this way frequently arises a tuberculosis of corpora lutea. Unruptured larger follicles appear to be practically never invaded, though in one instance Cohn found a primordial follicle in process of transformation into a tubercle. Another method of invasion of the ovary is ingrowth from a tuberculous tube through the hilus by way of the lymphatics, though this probably occurs less frequently than direct extension through the surface. Hematogenic invasion Cohn considers to be much less frequent than has been assumed. As a result of these pathological investigations, Cohn concludes that in operations for adnexal tuberculosis the ovaries should be conserved as far as possible, even if tuberculous patches are found on the surface; they are, however, to be removed if tuberculous infection of a corpus luteum, or evidences of invasion through the hilus are present.

---

**Histologic Changes in Myomas and Ovaries after the X-rays.**—ROBERT MEYER (*Zentralbl. f. Gyn.*, 1912, xxxvi, 529) has examined six myomatous uteri which had been removed on account of hemorrhage, after ineffectual x-ray treatment, to determine whether any definite changes had been produced by the treatment. He acknowledges that the series is too small to permit of any sweeping conclusions, but says that, although he discovered no absolutely distinctive lesions, one condition was found with such regularity, and in such a striking degree, that he feels some weight must be attached to it. This was a marked sclerosis of the myomas; it was present in all cases in high grade, but was especially remarkable in one case, in which only a few tumors, none larger than a cherry, were present. In these the muscle parenchyma had undergone almost complete atrophy, in many instances practically nothing being left of it beyond a few small scattered cell bundles; the ground-substance, consisting of fibrillæ, showed sclerosis and hyaline degeneration, the fibrillæ being in many instances much

thickened. Throughout this tissue were many small bloodvessels, whose walls were much better preserved than the surrounding tissue, almost suggesting in places an angiomatous condition. The outer coats of the vessels, especially the adventitia, had also suffered somewhat, however. The normal myometrium surrounding the tumors presented a marked contrast, being well preserved, and showing practically no sclerosis. Meyer says that while of course sclerosis is very commonly found in myomas, especially in those of considerable size, he has never before seen anything like such an extensive process in such small tumors as in this instance, which was all the more remarkable in that the patient was still in the period of sexual activity. He considers that this case lends considerable weight to the theory of a selective action exerted by the  $x$ -rays on myomatous tissue. In the ovaries Meyer found only the changes that have been repeatedly described as resulting from Röntgen treatment, degeneration of the ova, and a reduction in the number of follicles. These changes were found constantly, however, in the five pairs of ovaries examined, in one case these organs not having been removed. The fact that, in spite of these at times very considerable anatomical changes produced by the  $x$ -rays, not all cases of uterine hemorrhage are benefited by them, indicates, he says, that many as yet unexplained causes for this condition will, in the future, have to be taken into account.

---

**Radical Operation for Primary Carcinoma of the Vagina.**—A purely perineal operation for this condition, permitting removal of the entire genital tract with the rectum en bloc in an aseptic but thoroughly radical manner, has been recently described by PAUNZ (*Zentralbl. f. Gyn.*, 1912, xxxvi, 508). His patient was a woman, aged fifty-one years, who had borne eleven children, and who had a circular carcinomatous patch the size of a dollar on the posterior vaginal wall, adherent to the rectum. The chief points in favor of Paunz's operation, the detailed technique of which is given in the original article, as compared with other similar ones that have been described, are as follows. He began by making a circular incision around the vagina at the level of the external urinary meatus, and then closed both the vaginal and anal openings with silk, tying the ends of the sutures together, and leaving them long to use as tractors. Then by making a longitudinal incision from the posterior edge of the anus to the sacrum, extirpating the coccyx, and cutting through on both sides the entire pelvic diaphragm, the further carrying out of the operation was greatly facilitated. In this manner the entire pelvic floor was laid free from the urethra to the sacrum, so that it was possible to extirpate the entire vagina, the uterus with adnexa, the parametria, and the rectum in the most radical manner with almost perfect hemostasis, and without danger of infection or of implantation of malignant tissue, since neither the vagina nor rectum were opened during the entire operation. The only objection which Paunz can see to this type of operation is that the sphincter is sacrificed, and an artificial anus sacralis must be formed. He believes, however, that any attempt to preserve the sphincter, by merely resecting the rectum and bringing down the remaining bowel to it, complicates the operation too much, necessitating opening the intestine, and thereby robbing the procedure of its completely aseptic character. He con-

siders, therefore, that it is better to sacrifice the sphincter, especially as the patients gradually accustom themselves to the new conditions, by proper regulation of diet are able to secure but one stool a day, and are practically as comfortable as though they had a functioning sphincter muscle. The operation described by Paunz was carried out entirely under spinal anesthesia; the patient stood it extremely well, was out of bed the next day, and was discharged with the wound entirely healed at the end of four weeks.

---

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

---

UNDER THE CHARGE OF  
J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA.

---

**Varix Involving the Soft Palate, the Left Tonsil, and the Pharyngeal Wall.**—PORTER reports (*Jour. Lar., Rhinol., and Otol.*, February, 1912) a case which occurred in a married woman, aged forty-four years, complaining of inability to work or to walk much, owing to shortness of breath. She had also great difficulty in putting on her boots or stooping, as this caused a choking sensation. She stated that she has had varicose veins in the legs and vulva since the birth of her first child when she was seventeen years old. She has also a small angioma on the left little finger. Her grandfather and her mother suffered from varicose veins, and her eldest daughter, aged twenty-two years, was also affected in a similar way. The condition of her throat was first noticed by chance some sixteen years ago, at which time she was able to do her housework and no treatment was instituted. During the last eighteen months the symptoms have become greatly aggravated. On inspecting the pharynx a tortuous mass of veins was seen on the uvula, the left tonsil, the posterior pillar, and the wall of the pharynx. A blue, slightly raised area was also seen on the soft palate which overlies a second mass of veins. The larynx and rhinopharynx were healthy.

**Retro-pharyngeal Abscess with Paralysis of the Esophagus.**—THOMPSON reports (*Laryngoscope*, November, 1911) the case in a well-developed farmer's boy, aged nineteen years, who suddenly became unable to swallow after a few days' malaise, the inability continuing for one week, and being complicated by severe attacks of cough and dyspnea. Ultimately, a retropharyngeal abscess was ruptured by passing the finger into the rhinopharynx through a mass of inflamed adenoid tissue, after which the patient was fed through a stomach tube for three weeks and his further recovery was rapid. An abscess under a mass of adenoids, causing paralysis of the esophagus, had been seen by the doctor only once in twenty-seven years of throat-work.

**Brain Abscess, Secondary to Ethmoiditis and Frontal Sinusitis.**—McCoy (*Laryngoscope*, November, 1911) gives a final report of a case which he had reported a year previously in a boy, aged ten years, whose frontal sinus had been exposed through a Killian incision. The frontal sinus had been relieved of considerable pus and thoroughly curetted, together with some anterior ethmoidal cells, and the frontal nasal duct had been enlarged. Some weeks later it became necessary to expose a large epidural abscess leading down to and connecting with the frontal sinus, requiring the removal of considerable necrotic bone. After various tribulations, the patient succumbed a year after the operative procedure.

---

**Ethmoidectomy for Epithelioma.**—AUDIBERT reports (*Revue Hebdomadaire de Laryngologie, d'Otologie et de Rhinologie*, February 24, 1912) this case in a man, aged fifty-five years, unable to breathe through the right nasal passage, but without any other symptom of distress. The passage was found filled with cauliflower excrescences which bled at the slightest contact with the probe. Posterior rhinoscopy revealed pretty much the same aspect, and digital exploration detected a soft vegetative mass covering the rhinopharynx, the right choana, and reaching from the roof to the soft palate, barely passing the middle line, and consequently leaving a free space upon the right side. On diaphanoscopy, the frontal maxillary sinuses became illuminated normally. The mass was removed by external access with a good deal of hemorrhage, necessitating several tamponings. The middle and the superior turbinates were destroyed, the anterior ethmoidal cells resected to the cribriform plate of the ethmoid, and the septum was resected in its posterior portion. Every suspicious surface was thoroughly curetted, and hemorrhage arrested by tamponing the nasal fossæ with iodoform gauze, and the skin wound united with sutures. Recovery was good. Fifteen months later the patient still respired freely, and his nasal fossa did not exhibit any trace of the growth.

---

**Carcinoma of the Rhinopharynx.**—BROWN reports a case (*Laryngoscope*, November, 1911) in a man, aged forty-nine years, who for six months had been gradually losing flesh and strength, and complained likewise of a yellow discharge from the throat and nose, bad taste in the mouth, and breath offensive to his friends. On examination, February 26, 1911, a profuse purulent discharge was noticed in the inferior meatus on the left side, and posterior rhinoscopy revealed a large cauliflower-like mass almost completely filling the rhinopharynx and springing from the vault, principally on the left side. Microscopic examination of a section showed it to be a squamous-celled carcinoma. April 3, the patient complained of numbness of the left side of the face, and about four days later anesthesia of the parts supplied by the ophthalmic branch was nearly complete. April 18, upon awakening, the patient noticed double vision, and three days later ptosis was observed on this left side. On April 20, ptosis was complete. Death occurred May 6, the result of meningitis. As Brown observes, the consecutive history of the case is interesting in so plainly demonstrating the steady progress of the lesion.

**Laryngeal Carcinoma of Slow Evolution.**—KAHLER reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Pharynx*, February, 1912) a patient with carcinoma of the hypopharynx who had been submitted to an endolaryngeal operation ten years previously, not impossibly for a cancer of the larynx of slow evolution. He also reported a case in a man, aged fifty-two years, who had for eight and one-half years presented a clinical aspect which did not permit a diagnosis of carcinoma of the larynx. The biopsy alone, made several times, indicated the diagnosis of carcinoma. An analogous case showed how important it was to be prudent as to the indication for a radical operation by external procedure, in which the mortality is large.

---

## PATHOLOGY AND BACTERIOLOGY

---

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME  
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT;  
SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

---

**The Destruction of Red Blood Corpuscles.**—I. I. LINTVAREV (*Ann. de l'Inst. Past.*, January and February, 1912, Tome xxvi, Nos. 1 and 2) deals at some length with the intrasplenic and intrahepatic destruction of red blood corpuscles. Under normal conditions the destruction of blood occurs by the agency of special cells, the erythrophages, which are partly destroyed in the spleen itself, but are, for the most part, carried to the liver by the blood where they hand over at their destruction, to the liver cells, the products of destruction of the red corpuscles. Meanwhile, the bone marrow replaces the destroyed corpuscles. In pathological states characterized by the symptoms of the primary anemias, so-called, the destruction of red corpuscles by these erythrophages is greatly increased. Thus Lintvarev would group together Banti's disease, cirrhosis of the liver, splenomegaly, and pernicious anemia, which differ from one another merely in a quantitative way and in the organs in which the most marked changes occur: Pernicious anemia, if the marked changes are in the blood picture; hepatic cirrhosis if the connective tissue of the liver is most affected; splenomegaly, if the enlargement of the spleen appears to surpass in importance the hepatic and blood disturbances. Cirrhosis of the liver results, Lintvarev thinks, from irritation of the tissue of Glisson's capsule by the products of disintegration of the erythrophages and their contents, which also is responsible, in other cases, for the stimulation of the splenic connective tissue. The erythrophages are produced in the Malpighian corpuscles of the spleen, as well as in lymph nodes, and certain poisons, exogenous as well as endogenous, are responsible for an excessive production of these cells. The primary anemias are characterized by such an excess, with increased destruction

of the red corpuscles due to the heightened activity of the destroyers: as a result of the destruction, and the great need of new corpuscles, the blood shows young and often immature forms of corpuscle. Lintvarev sees in the overproduction of phagocytes in tuberculous and syphilitic states, the main cause of the anemia produced, as well as the lesions of spleen and liver to which reference has been made. The happy term "*phagocytes à tout faire*" is employed to designate the erythroblasts.

---

**Experimental Goitre and Cardiac Hypertrophy from Suspected Water Sources.**—BIRCHER (*Deutsch. Zeitschr. f. Chir.*, 1911, cxii, Nos. 4 to 6) has demonstrated the possibility of causing struma in rats by causing them to drink water of the particular geological sources that are known to cause it in human beings. His series embraced 120 animals, was carefully controlled, and consisted of animals from various districts. Against 120 successful attempts in producing goitre, there was not a single tumor found in the control animals, and histological examination leads Bircher to state that the conditions are strictly parallel. With continuance of the use of the water concerned the cellular degenerations were readily observed; nodular and diffuse change were observed in the thyroid, and hypertrophy of the heart accompanied by degeneration in its muscle.

---

**Typhoidal Bacteriemia with Localization in the Lung.**—That we do well to consider typhoid fever as a bacteriemia with localization in the intestine is evidenced by a case carefully reported by COURMONT, SAVY, and CHARLET (*Jour. de Physiol. et de Path. Générale*, March 15, 1912, xiv, No. 2) in which there were no intestinal symptoms, but a continued and severe purulent bronchitis. The malady began in a woman, aged thirty-eight years, with continued fever, torpor, enlarged spleen, and a slight ulceration on one anterior pillar of the pharynx. A very irregular fever, with large regressions, lasting more than three months, followed. The pulse was rapid, and the pulmonary symptoms marked; purulent sputum was present in great quantity; there was frequent cough, dyspnea without cyanosis, no consolidation, but numerous rales in all parts of the lungs. Albuminuria was marked. Headache and diarrhea were absent, the tongue was furred but the appetite continued fairly good. Blood cultures, at first unsuccessful, later at various times gave the bacillus typhous, typical even in agglutination. Later, the bacteria appeared in the urine. The Widal reaction appeared on the eighth day. No rose spots were seen at any time. A large bed sore occurred. After a desperate illness, during the course of which the patient was operated upon for strangulation of a preëxistent hernia, she made a perfect recovery.

---

**Antityphoidal Immunization by the Intestinal Tract.**—COURMONT and ROCHAIX previously demonstrated the possibility of antityphoidal immunization in animals by the intestinal route, and have now applied it to man (*Jour. de Phys. et de Path. Gén.*, xiv, No. 2). The vaccine was given, with laudanum, by the rectum, and in no case was there any bodily reaction. In the blood, the agglutinative, bacteriolytic, and bactericidal properties appeared in due time, attaining their maximum three weeks after the first of three injections at intervals of five days.

The agglutinative and bacteriolytic powers were surpassed by the bactericidal, and the three varied from time to time, the curves not being parallel; all were demonstrable six months later, although attenuated: they soon disappeared thereafter. The time of their appearance and their duration were about the same as in subcutaneous inoculation, but the degree of power was scarcely so high.

**The Source and Development of Generalized Tuberculosis.**—JURGELUNAS (*Zeits. f. Hyg. u. Infekt.*, lxxi, Hft. 2), publishes an extensive series of experiments upon the vexed question of the routes by which tubercle bacilli enter the organism. His results conform in general to what are the most widely accepted ideas. Guinea-pigs exposed to the inhalation of dry and moist cultures showed implication first of the thoracic organs, whose infection was both direct and also indirect through the walls of the mouth cavity and throat. Infection occurred alike easily if moist or dried cultures were used. Through these walls, the quickest mode of infection was the introduction of emulsion of bacilli into the mouth; while from the lumen of the intestine the disease could be readily caused if a great number of bacilli were introduced. The introduction of an emulsion of bacilli of the human type into the intestine failed to infect; on the contrary, infection was obtained by the introduction of an emulsion of bovine bacilli, especially by way of the mouth and throat: bovine bacilli were apparently able to infect from the intestine only if a large quantity was used. Human bacilli in the mouth cavity of sucking pigs, goats, and sheep failed to infect, while bovine bacilli succeeded readily under like circumstances. In the above mentioned animals, the unwounded wall of the gastrointestinal tract seemed to be a strong, but not insurmountable barrier against the passage of bacilli: the appendix and the sacculus rotundus of the rabbit showed the weakest resistance. Jurgelunas feels justified in reasserting strongly the nonidentity of human and bovine types of the bacillus, and considers the rabbit and the sucking pig as the best subjects for their differentiation.

**A New Japanese Publication.**—We welcome the appearance of the first volume of the Proceedings of the Japanese Pathological Association, which met in April, 1911, in Tokyo. The Proceedings appear, some in German, some in English, and the greater part in Japanese. The main general subject discussed was "*Schistosomiasis japonica*," to which a symposium was devoted.

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL*.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript*.

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

# CONTENTS

## ORIGINAL ARTICLES

- A Clinical Study of a Thousand Cases of Ulcer of the Stomach and Duodenum . . . . .** 157  
By JULIUS FRIEDENWALD, M.D., Professor of Gastro-enterology in the College of Physicians and Surgeons, Baltimore.
- Diarrhea of Gastric Origin: Diagnosis and Treatment . . . . .** 170  
By DOUGLAS VANDERHOOF, A.M., M.D., Consulting Physician to the Johnston-Willis Sanatorium and Attending Physician to the Memorial Hospital, Richmond, Va.
- Multiple Subcutaneous Hemangiomas, Together with Multiple Lipomas, Occurring in Enormous Numbers in an Otherwise Healthy Muscular Subject . . . . .** 189  
By JOHN T. BOWEN, M.D., Edward Wigglesworth Professor of Dermatology, *Emeritus*, Harvard University.
- Malignant Disease of the Lung with Special Reference to Sarcoma . . .** 193  
By A. A. STEVENS, M.D., Professor of Therapeutics and Clinical Medicine, Woman's Medical College of Pennsylvania; Lecturer in Medicine, University of Pennsylvania, etc.
- Paroxysmal Hemoglobinuria . . . . .** 203  
By ROBERT A. COOKE, M.D., New York.
- A Case of Delayed Development in a Boy Treated with Thymus Gland . .** 219  
By C. G. KERLEY, M.D., Professor of Pediatrics in the New York Polyclinic and Hospital, and S. P. BEEBE, M.D., Professor of Experimental Therapeutics, Cornell University Medical College, New York.
- Acute Pancreatitis . . . . .** 221  
By JOSEPH M. KING, M.D., Physician to the Sisters' Hospital, Los Angeles, California.
- The Effect of Cold Air upon the Circulation in Healthy and Sick Individuals . . . . .** 233  
By THEODORE B. BARRINGER, JR., M.D., Associate Attending Physician, New York Hospital.
- Leukocyte and Differential Counts in Ward and Open Air Treatment . .** 238  
By T. G. ORR, M.D., House Physician, New York Hospital (House of Relief).
- Fatal Pneumothorax Following Exploratory Puncture . . . . .** 241  
By HUGHES DAYTON, M.D., Associate Attending Physician, New York Hospital.
- Tuberculin Therapy in Surgical Tuberculosis . . . . .** 245  
By THOMAS WOOD HASTINGS, M.D., Professor of Clinical Pathology in the Cornell University Medical College, New York.



## REVIEWS

Duodenal Ulcer. By B. G. A. Moynihan, M.D. (Lond.), F.R.C.S. . . . .	271
Surgery and Society; A Tribute to Listerism. By C. W. Saleeby, M.D., F.R.S.E. . . . .	272
A Treatise on Tumors. For the Use of Physicians and Surgeons. By Arthur E. Hertzler, M.D. . . . .	274
Laboratory Manual of Physiology. By Frederick C. Busch, B.S., M.D. . . . .	275
Pathologische Anatomie: ein Lehrbuch für Studierende und Aerzte. Herausgegeben von L. Aschoff . . . . .	276
Die Störungen des Verdauungsapparates als Ursache und Folge anderer Erkrankungen (The Disturbances of the Digestive Apparatus as the Cause and Consequence of Other Diseases). By Dr. von Hans Herz . . . . .	280
Cesarean Section in Great Britain and Ireland. By Armand Routh, M.D., F.R.C.P. . . . .	281
A Mother's Guide. A Manual for the Guidance of Mothers and Nurses. By Francis Tweddell, M.D. . . . .	283
Ophthalmic Myology. A Systematic Treatise on the Ocular Muscles. By G. C. Savage, M.D. . . . .	284
Manual of Practical Physiology. By John C. Hemmeter, M.D., Ph.D., LL.D. . . . .	284

## PROGRESS OF MEDICAL SCIENCE

## MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

The Successful Inoculation of Blood, Blood Serum, and Sperm of Syphilitics into Rabbits . . . . .	285
An Epidemic of Sore Throat Due to a Peculiar Streptococcus . . . . .	286
Pericarditis in Bright's Disease; Its Relation to Nitrogen Retention . . . . .	286
The Relative Value of Immediate and Delayed Laparotomy in Pneumococcal Peritonitis . . . . .	286
The Relation of Chorea to Rheumatism; An Analysis of 300 Cases . . . . .	287
The Causes of Death in Tabes . . . . .	287
The Value of the Antigen Reaction of Debré and Paraf for Rapid Diagnosis of Urinary Tuberculosis . . . . .	288
On the Lesions Produced in the Appendix by Oxyuris Vermicularis and Trichocephalus Trichiura . . . . .	288
The Avoidance of Anaphylactic Phenomena on the Injection of Immune Serum . . . . .	289
Urobilin and Bilirubin in Human Blood Serum . . . . .	289
On the Determination of Urea in the Urine . . . . .	290
Painting the Peritoneum with Tincture of Iodine in Tuberculous Peritonitis . . . . .	290

**SURGERY**

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

Evidence of Occult Blood in the Stools and Stomach Contents and its Relation to the Diagnosis of Surgical Conditions of the Stomach, Especially for the Early Diagnosis of Gastric Carcinoma . . . . .	291
A Contribution on the Transplantation of Bone . . . . .	291
Low Position of the Transverse Colon . . . . .	292
Paralysis after the Use of Esmarch's Tourniquet . . . . .	292
Hematuria of Nephritis and Renal Papillitis from a Surgical Standpoint: A Study of 73 Cases . . . . .	293
The Technique of Paravertebral Nerve Anesthesia . . . . .	294

**THERAPEUTICS**

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Calcium Salts in the Treatment of Asthma . . . . .	295
Normal Human Blood Serum Injections in Melena Neonatorum and other Conditions . . . . .	295
Camphor and Pneumococci . . . . .	296
The Treatment of Melena Neonatorum by Human Blood Serum . . . . .	296
Untoward Results from Transfusion of Blood in Pernicious Anemia . . . . .	296
Vaccine Therapy in Rheumatoid Arthritis . . . . .	297
Subcutaneous Injection of Small Quantities of Human Blood in Spontaneous Hemorrhage of Newborn . . . . .	297
The Results of Anti-typhoid Vaccination in the Army in 1911, and Its Suitability for Use in Civil Communities . . . . .	298
Tincture of Digitalis—Its Potency and Keeping Properties . . . . .	299

**PEDIATRICS**

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

The Treatment of Chorea Minor . . . . .	299
Duration of the Infectious Period in Scarlet Fever . . . . .	300
Significance of the Facialis Phenomenon in Later Childhood . . . . .	301

**OBSTETRICS**

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

The Cause of Rupture in Tubal Pregnancy . . . . .	302
The Prevention of the Formation of Striæ of Pregnancy . . . . .	302
Medical Education and the Midwife Problem in the United States . . . . .	303

**GYNECOLOGY**

UNDER THE CHARGE OF

**JOHN G. CLARK, M.D.**

Vaginal Hysterectomy under Local Anesthesia . . . . .	305
Lymphatics of the Clitoris . . . . .	306
Composition of the Menstrual Fluid . . . . .	306
Arsenic as a Factor in Menstruation . . . . .	307

**DERMATOLOGY.**

UNDER THE CHARGE OF

**LOUIS A. DUHRING, M.D., AND MILTON B. HARTZELL, M.D.**

A Cryptogamic Parasite Found in a Dermatosiis of the Type of Pityriasis Rosea . . . . .	308
Bullous Antipyrine Eruptions of the Buccal Cavity . . . . .	308
Skin Changes in Leukemias . . . . .	308
Bullous Eruption Associated with Appendix Abscess . . . . .	309
Treatment of Acne by Vaccines . . . . .	309
Seven Hundred Consecutive Cases of Tinea Capitis . . . . .	309
Treatment of Erysipelas . . . . .	309
A Case of Phenol (Carbolic Acid) Gangrene . . . . .	309

**PATHOLOGY AND BACTERIOLOGY**

UNDER THE CHARGE OF

**JOHN McCRAE, M.D., M.R.C.P.**

The Formation of Pigment . . . . .	310
Experimental Measles in Monkeys . . . . .	310
A New Anaërobic Bacillus in Typhoid Stools . . . . .	311
Pneumococcus Influenza . . . . .	311
The Detection of Horse Flesh in Sausages . . . . .	311
The Local Effect of Orchitis in Mumps . . . . .	312
Trichiniasis . . . . .	312

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

AUGUST, 1912

ORIGINAL ARTICLES

A CLINICAL STUDY OF A THOUSAND CASES OF ULCER OF  
THE STOMACH AND DUODENUM.<sup>1</sup>

BY JULIUS FRIEDENWALD, M.D.,

PROFESSOR OF GASTRO-ENTEROLOGY IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
BALTIMORE

IN the study of the thousand cases of ulcer of the stomach and duodenum, great care has been exercised to eliminate all cases in which there has been the slightest question as to the diagnosis, and suspected cases in which the diagnosis has been the least doubtful have been excluded from this report. The thousand cases occurred in 12,598 patients effected with various gastric disturbances (7.8 per cent.).

AGE. As is observed in the following table, the largest proportion of cases occur between the twentieth and fiftieth years and the greatest number between the twentieth and thirtieth years:

Age.	Cases.	Per cent.
0 to 10 . . . . .	2	0.20
10 to 20 . . . . .	162	16.20
20 to 30 . . . . .	345	34.50
30 to 40 . . . . .	229	22.90
40 to 50 . . . . .	128	12.50
50 to 60 . . . . .	93	9.30
60 to 70 . . . . .	38	3.80
Over 70 . . . . .	3	0.30

SEX. Of the total number of cases there are 676 males and 324 females. The following table illustrates the number of cases observed in males and females according to age:

<sup>1</sup> Presented at the Meeting of the Association of American Physicians, held at Atlantic City, May 14, 1912.

Years.	Males.	Females.	Total.
0 to 10 . . . . .	2	0	2
10 to 20 . . . . .	124	38	162
20 to 30 . . . . .	262	83	345
30 to 40 . . . . .	119	110	229
40 to 50 . . . . .	91	37	128
50 to 60 . . . . .	48	45	93
60 to 70 . . . . .	29	9	38
Over 70 . . . . .	1	2	3

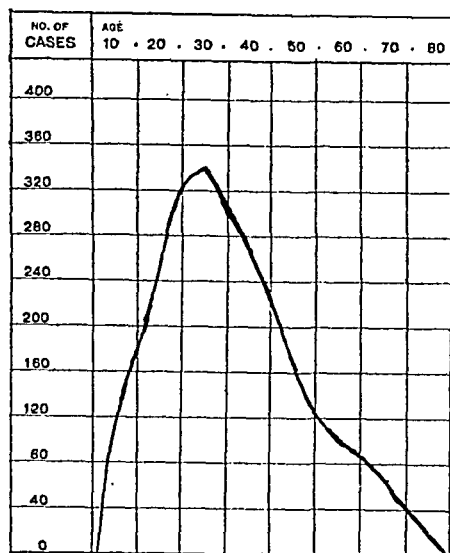


FIG. 1.—Age diagram of 1000 cases of ulcer.

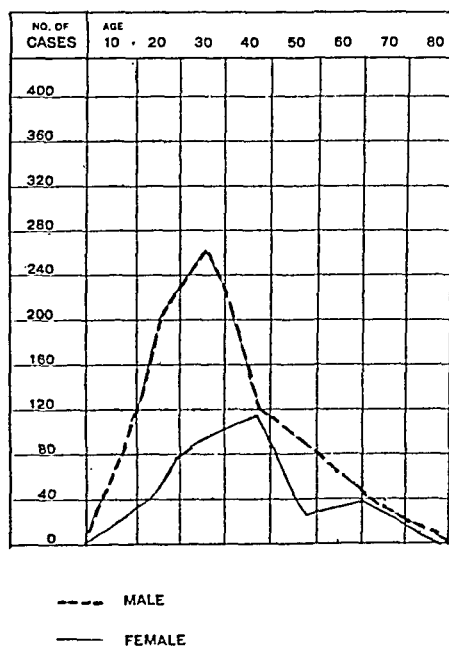


FIG. 2.—Sex and age diagram of 1000 cases of ulcer.

Of the 1000 cases, 31 were found in cooks, 18 in workers in metals, 12 in workers in porcelain, 8 were miners, 28 were tailors, 15 were shoe makers, and 19 were blacksmiths.

A definite history of trauma was elicited in 23 cases, in 10 of which there had been blows on the abdomen.

**ANEMIA.** In 324 of our cases in which hemoglobin estimations had been recorded, anemia was present in 211 cases (65 per cent.). The average of the hemoglobin estimations was 61 per cent.; this does not, however, include those cases accompanied by severe hemorrhages. In 302 cases in which hematemesis or melena occurred, the average hemoglobin estimation was 46 per cent.

**CARDIAC AND VASCULAR CHANGES.** Chronic endocarditis was present in 43 cases (4.3 per cent.); arteriosclerosis in 153 (15.3 per cent.).

**PREVIOUS DISORDERS OF DIGESTION.** In the 1000 cases there was a history of some previous digestive disturbance in 482 cases (48.2 per cent.). Some of these disturbances must have been premonitory symptoms of the ulcer itself, inasmuch as there is often great difficulty in distinguishing early signs of ulcer from ordinary slight gastric disturbances.

**EXCESSES IN FOOD AND DRINK.** The history of former indiscretions in diet was obtained in 433 instances (43.3 per cent.); but only in 129 (12.9 per cent.) did the patient attribute his disease to some specific error in diet.

A history of alcoholism was obtained in 214 instances (21.4 per cent.).

**INFECTIOUS DISEASES.** A history of syphilis was obtained in 52 instances, yet only in 5 could the ulcer be directly attributed to this disease. Tuberculosis of the lungs was present in 26 instances, but as far as could be observed this disease appeared to have no etiological bearing upon the production of the ulcer.

**THE GASTRIC SECRETION IN ULCER.** Of the thousand cases the gastric secretion was examined in 810 instances.

	Cases.	Per cent.
Normal acidity was observed in . . . . .	376	46.4
Hyperchlorhydria was observed in . . . . .	246	30.3
Hypochlorhydria and anacidity . . . . .	188	23.2
	<hr/>	
	810	

Of the 810 cases, consisting of 516 males and 294 females, the acidities were as follows:

	Males.		Females.	
	Cases.	Per cent.	Cases.	Per cent.
Normal acidity . . . . .	271	33.5	105	12.9
Hyperchlorhydria . . . . .	161	19.8	85	10.5
Hypochlorhydria and anacidity . . . . .	84	10.4	104	12.8
	<hr/>		<hr/>	
	516		294	

Hyperacidity was proportionately more frequently observed in males and subacidity in females, while the greatest number of males as well as females presented a normal acidity. It is interesting to note the relation of acidities to the duration of the disease. In acute ulcers and especially those accompanied by recent hemorrhages, the acidity is very high, while in chronic forms the acidity is low. In 128 cases of acute ulcer of which 75 were males and 53 were females, 96 (61 males and 35 females), presented high acidities.

	Males.		Females.	
	Cases.	Per cent.	Cases.	Per cent.
Normal acidity . . . . .	12	9.3	8	0.6
Hyperchlorhydria . . . . .	61	47.6	35	27.3
Hypochlorhydria . . . . .	2	1.6	10	7.7
	<hr/> 75		<hr/> 53	

Of the 426 cases of chronic ulcers of long duration the tendency is toward low acidities. The following table illustrates this condition:

	Males.		Females.	
	Cases.	Per cent.	Cases.	Per cent.
Normal acidity . . . . .	94	22.0	85	19.9
Hyperchlorhydria . . . . .	35	8.3	39	9.1
Hypochlorhydria . . . . .	80	18.6	93	21.8
Total . . . . .	<hr/> 209	<hr/> 48.9	<hr/> 217	<hr/> 50.8

**DURATION OF SYMPTOMS.** The average duration of symptoms in ulcer is twelve years. The following table illustrates the average duration of symptoms in males and females according to age:

Age.	Males.	Average duration of symptoms in years.	Females.	Average duration of symptoms in years.
0 to 10 . . . . .	2	$\frac{1}{2}$	0	
10 to 20 . . . . .	124	2	38	$1\frac{1}{2}$
20 to 30 . . . . .	262	11	83	$10\frac{1}{2}$
30 to 40 . . . . .	119	19	110	$13\frac{1}{2}$
40 to 50 . . . . .	91	14	37	16
50 to 60 . . . . .	48	$16\frac{1}{2}$	45	19
60 to 70 . . . . .	29	17	9	$19\frac{1}{2}$
Over 70 . . . . .	1	20	2	12

**PAIN.** Pain, the most prominent feature of ulcer was present in 94 per cent. of our cases. It is most prominent in those cases accompanied by hyperchlorhydria. Of the 810 cases in which the gastric contents was analyzed the relation of pain to acidity is presented in the following table, from which it is evident that pain is most pronounced in those instances associated with high acidity:

	Absent.			Moderate.		Moderately severe.		Severe.	
	Cases.	No.	%	No.	%	No.	%	No.	%
Normal acidity . . . . .	376	2	0.2	92	11.3	123	15.1	159	19.6
Hyperchlorhydria . . . . .	246	1	0.1	8	9.0	35	4.3	202	24.9
Hypochlorhydria . . . . .	188	7	0.7	59	7.3	82	10.1	40	5.0

**TIME OF APPEARANCE OF PAIN.** Of the 1000 cases the pain appeared within the first hour after meals in 223 instances, between one and two hours in 188, after two hours in 491, and in 38 it appeared irregularly.

**EFFECT OF FOOD UPON PAIN.** The pain was aggravated in 212 instances by the ingestion of food and was relieved in 619 instances by the taking of food. In 109 instances the pain was neither increased nor relieved by the taking of food.

**INTERMISSIONS OF PAIN.** In 563 instances of the 940 cases in which pain was present, there were one or more periods in which distinct intermissions of pain occurred varying from one to twelve months or more. The following table presents these according to periods of intermission in months:

Cases.	Months of intermission.
94 . . . . .	1 to 2
72 . . . . .	2 to 3
82 . . . . .	3 to 4
79 . . . . .	4 to 5
48 . . . . .	5 to 6
26 . . . . .	6 to 7
38 . . . . .	7 to 8
34 . . . . .	8 to 9
17 . . . . .	9 to 10
20 . . . . .	10 to 11
31 . . . . .	11 to 12
22 . . . . .	12 or more.

---

563

**TENDERNESS.** Of the 1000 cases epigastric tenderness was present in 908 cases (90.8 per cent.). A tender area was noted to the right of the median line in 41 cases (4.1 per cent.). The dorsal together with an epigastric tender spot, was noted in 523 instances (52.3 per cent.). A dorsal area alone in 25 (2.5 per cent.). No tender area in 26 instances (2.6 per cent.).

**VOMITING.** Vomiting is another very prominent symptom, though not as constant as the pain. It occurred in 676 of our cases (67.6 per cent.). It is proportionately more frequent in those instances in which pain appears early. Of the 940 cases in which pain was present there were 223 having pain within the first hour, of which 194 had vomiting. There were 188 with pain between the first and second hours, of which 143 had vomiting; 529 manifested pain two hours after meals, (or pain appeared irregularly), of which 324 had vomiting. The following table illustrates this condition:

Time of appearance of pain in hours.	Cases with pain.	Cases with vomiting.	General per cent.	Per cent. of cases of vomiting in propor- tion to the cases with pain.
In one hour . . . . .	223	194	29.3	87.0
In one to two hours . . . . .	188	143	21.6	76.6
After two hours or irregularly .	529	324	49.0	61.2
Total . . . . .	940	661		



Of the 40 cases of ulcer not accompanied by pain, vomiting occurred in 16 cases (40 per cent.).

**VOMITING AND ACIDITY.** Of the 810 cases in which an examination was made of the gastric contents, the relation of the vomiting to the acidity is illustrated in the accompanying table. There were 676 of these cases in which vomiting was present. Of these there were 531 in which analyses were made. Vomiting is definitely more prominent in those instances accompanied by high acidity.

Acidity.	Cases.	Moderate vomiting.		Severe vomiting.	
		Number.	Per cent.	Number.	Per cent.
Normal acidity . . . . .	298	125	23.5	171	32.5
Hyperchlorhydria . . . . .	138	18	3.3	122	22.8
Hypochlorhydria . . . . .	95	76	14.3	19	3.5

**HEMATEMESIS.** Gastric hemorrhage was manifested or a history of this symptom was presented in 228 of the 1000 cases, that is in 22.8 per cent. In the following table the proportion of cases accompanied by a single hemorrhage or with multiple hemorrhages are presented according to age:

Years.	Cases with hemorrhage.	Per cent. of cases with hemorrhage.	Proportion cases single hemorrhage.		Proportion cases multiple hemorrhage.	
			Number.	Per cent.	Number.	Per cent.
0 to 10 . . . . .	0	0.0	0	0.0	0	0.0
10 to 20 . . . . .	48	21.0	17	7.4	31	13.6
20 to 30 . . . . .	81	35.5	23	10.0	58	25.4
30 to 40 . . . . .	42	18.3	28	12.7	13	5.7
40 to 50 . . . . .	29	12.8	8	3.4	21	9.0
50 to 60 . . . . .	20	8.8	6	2.6	14	6.0
60 to 70 . . . . .	8	3.5	6	2.6	2	0.9
Over 70 . . . . .	0	0.0	0	0.0	0	0
Total . . . . .	228	99.6	89	38.7	139	60.6

**MELENA.** Tar-colored stools or a history of this condition was presented in 515 of the 1000 cases, that is 51.5 per cent. The following table illustrates the number and percentage of these cases at various ages; the largest proportion appearing between the tenth and thirtieth years:

Years.	Cases with melena.	Per cent. of cases with melena.
0 to 10 . . . . .	0	0.0
10 to 20 . . . . .	103	10.3
20 to 30 . . . . .	161	16.1
30 to 40 . . . . .	98	9.8
40 to 50 . . . . .	66	6.6
50 to 60 . . . . .	61	6.1
60 to 70 . . . . .	24	2.4
Over 70 . . . . .	2	0.2
Total . . . . .	515	51.5

It is also interesting to note the proportion of cases with melena, and to compare this condition with hematemesis observed at various

ages, as is illustrated in the accompanying table. Melena is over twice as frequent as gastric hemorrhage and occurs much more frequently after the fortieth year of age than is observed with hematemesis.

COMPARISON OF CASES WITH HEMATEMESIS AND MELENA AT VARIOUS AGES.

Ages.	Gastric hemorrhage.		Melena.	
	Cases.	Per cent.	Cases.	Per cent.
0 to 10 . . . . .	0	0.0	0	0.0
10 to 20 . . . . .	48	4.8	103	10.3
20 to 30 . . . . .	81	8.1	161	16.1
30 to 40 . . . . .	42	4.2	98	9.8
40 to 50 . . . . .	29	2.9	66	6.6
50 to 60 . . . . .	20	2.0	61	6.1
60 to 70 . . . . .	8	0.8	24	2.4
Over 70 . . . . .	0	0.0	2	0.2
	228		515	

There were 287 cases accompanied by melena without any evidence of hematemesis. These cases are presented according to age in the following table. They are cases of duodenal ulcers which are to be presented later on.

Age.	Cases.	Per cent.
10 to 20 . . . . .	55	19.5
20 to 30 . . . . .	82	28.3
30 to 40 . . . . .	56	19.5
40 to 50 . . . . .	37	12.9
50 to 60 . . . . .	41	14.2
60 to 70 . . . . .	16	5.5
Over 70 . . . . .	0	0.0
Total . . . . .	287	

**OCCULT BLOOD.** The test for occult blood was made constantly only with feces. The stools were examined in 539 cases of the 1000 cases. Of these 467 gave one or more positive results (86.6 per cent.). The examinations here noted were only made in those instances in which visible blood was absent, or had not appeared for a considerable length of time before the test had been made. Blood was not always present in the first test but frequently appeared sometime during the course of the disorder.

**EINHORN STRING TEST.** The string test was made in 41 of our cases and was found positive in 34 (83 per cent.). The results obtained by means of this test are about as sensitive as the test for occult blood.

**COMPLICATIONS.** Atony of the stomach was noted in 321 (32.1 per cent.) of our cases and enteroptosis was noted in 411 instances (41.1 per cent.). Evidences of dilatation of the stomach were observed in 336 instances (38.4 per cent.). A tumor was palpable in the form of an hypertrophied pylorus in 25 of our cases (2.5 per cent.), and perforation occurred in 10 cases (1 per cent.).

**DUODENAL ULCERS.** Of the 1000 cases of ulcer 529 were duodenal (52.9 per cent.), and 409 gastric (40.9 per cent.), and 62 (6.2 per cent.) undetermined. The largest number of duodenal ulcers occurred between the twentieth and thirtieth years. The following table illustrates the number of cases of duodenal ulcer arranged according to age:

Years.	Cases.	Per cent.
10 to 20 . . . . .	55	10.3
20 to 30 . . . . .	159	30.0
30 to 40 . . . . .	149	28.2
40 to 50 . . . . .	91	17.2
50 to 60 . . . . .	43	8.2
60 to 70 . . . . .	32	6.0
Over 70 . . . . .	0	0.0
	529	

**SEX.** The largest proportion of cases occurred in males, *i. e.*, 307 males (58 per cent.), and 222 females (42 per cent.). The following table indicates the number of males and females at various ages:

Years.	Males.		Females.	
	No.	Per cent.	No.	Per cent.
10 to 20 . . . . .	31	5.8	24	4.5
20 to 30 . . . . .	85	16.1	74	13.9
30 to 40 . . . . .	87	16.4	62	11.7
40 to 50 . . . . .	66	12.4	25	4.7
50 to 60 . . . . .	11	2.0	32	6.0
60 to 70 . . . . .	27	5.1	5	0.9
	307		222	

**ACIDITY.** Of the 529 cases the secretion was analyzed in 402. Of the 402 there were 195 with normal acidity, 142 with hyperchlorhydria, and 65 with hypochlorhydria. The accompanying table illustrates this condition:

	No.	Per cent.
Normal acidity . . . . .	195	48.5
Hyperchlorhydria . . . . .	142	35.3
Hypochlorhydria . . . . .	65	16.1
	402	

Of the 402 cases there were 213 males and 189 females which are arranged according to their acidities in the following table. Hyperacidity being more frequently observed in males and sub-acidity in females.

	Male.		Female.		Total.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Normal acidity . . . . .	120	29.7	75	18.6	195	48.3
Hyperchlorhydria . . . . .	79	19.6	63	15.6	142	35.2
Hypochlorhydria . . . . .	14	3.4	51	12.4	65	16.1

**PAIN.** Pain was present in 512 of our duodenal cases (96.5 per cent.). It was absent in 17 cases. It was most prominent in those cases with hyperacidity. Of the 402 cases in which the gastric contents were examined, the relation of the pain to the acidity is illustrated in the following table; the pain being more severe in those instances associated with high acidity:

		Absent.		Mild.		Moderately severe.		Severe.	
	Cases.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Normal acidity	195	1	0.2	45	12.1	59	14.6	90	22.1
Hyperchlorhydria	142	1	0.2	6	1.4	24	5.9	111	27.3
Hypochlorhydria	65	5	1.2	25	6.2	10	2.4	25	6.2

**INTERMISSIONS OF PAIN.** Of the 512 cases in which pain was present, 316 presented records showing distinct periods in which the pain had disappeared for a time; one month to twelve months or more (63 per cent.). The following table illustrates the number of cases presenting the intermissions of pain according to the number of months.

Cases,	Intermissions in pain in months.
53 . . . . .	1 to 2
36 . . . . .	2 to 3
44 . . . . .	3 to 4
37 . . . . .	4 to 5
34 . . . . .	5 to 6
17 . . . . .	6 to 7
23 . . . . .	7 to 8
29 . . . . .	8 to 9
9 . . . . .	9 to 10
15 . . . . .	10 to 11
14 . . . . .	11 to 12
5 . . . . .	12 or more.

**TENDERNESS.** Of the 529 cases epigastric tenderness was present in 474 cases (89.4 per cent.). A tender area to the right or left of the median line in 41 cases (7.7 per cent.). A dorsal tender area together with an epigastric spot was present in 289 cases (54.6 per cent.), and a dorsal tender area alone in 6 cases (1.1 per cent.), no tender area in 8 cases (1.5 per cent.).

**VOMITING.** Vomiting occurred in 113 of our duodenal ulcers, that is 21 per cent.

**VOMITING AND ACIDITY.** Of the 402 cases in which the gastric contents was analyzed the relation of the acidity to vomiting is as illustrated in the following table. There were 113 cases in which vomiting occurred, of which the gastric contents was examined in 92. It is here demonstrated that vomiting is more frequent in those cases accompanied by high acidity.

	No.	Moderate vomiting.		Severe vomiting.	
Normal acidity . . . . .	48	20	4.8	28	30.4
Hyperchlorhydria . . . . .	38	6	6.5	32	34.8
Hypochlorhydria . . . . .	6	5	5.4	1	1.0

**MELENA.** Tar-colored stools or a history of this condition appeared in 287 of our 529 cases, (54 per cent.). The following table presents the number of cases according to age.

Age.	Cases.	Per cent.
10 to 20 . . . . .	55	19.5
20 to 30 . . . . .	82	28.3
30 to 40 . . . . .	56	19.5
40 to 50 . . . . .	37	12.9
50 to 60 . . . . .	41	14.2
60 to 70 . . . . .	16	5.5

**OCCULT BLOOD.** Of the 529 cases, an examination of the feces was made in 381. Of this number, 315 presented one or more positive tests for occult blood (83 per cent.). The examinations here noted include those cases alone in which visible blood was entirely absent, or had not been present for a considerable length of time before the test for occult blood was made. The blood was frequently absent in the first examination but usually appeared sometime during the course of the disorder, and especially when the symptoms became aggravated. It gradually disappeared as recovery took place.

**RESULTS OF TREATMENT OF GASTRIC AND DUODENAL ULCERS.** Of the 1000 cases, 885 were under direct observation during the entire course of treatment. In the remaining 115, the diagnosis was simply made, treatment was not instituted, or if so, was only imperfectly carried out.

Of the 885 cases, 794 were treated medically and 91 surgically. Of the 794 treated medically, 20 were required to seek surgical aid later on account of the failure of medical treatment. Of the 794 treated medically, 521 undertook the rest cure treatment, while 273 were treated as ambulatory patients.

Of the 521 treated by the rest cure, 404 had the Leube treatment, and 117 the Lenhartz treatment, or a slight modification of the same. Of the 404 treated by the Leube, 291 or 72 per cent. were cured, 97 or 24 per cent. were not cured, and 16 or 4 per cent. died. Of the 117 treated by the Lenhartz treatment, 78 or 66 per cent. were cured, 34 or 29 per cent. were not cured, and 5 or 5 per cent. died.

Of the 273 cases treated as ambulatory patients, 153 were treated with nitrate of silver, 110 with subnitrate of bismuth, and 10 by the olive oil method. Of the 153 treated with the nitrate of silver, 73 or 47 per cent. were cured, while 80 or 53 per cent. were not cured. Of the 110 treated with subnitrate of bismuth, 56 or 50 per cent. were cured, while 54 or 49 per cent. were not cured. Of the 10 treated by the olive oil method, 4 or 40 per cent. were cured, while 6 or 60 per cent. were not cured. The following table illustrates the percentage of recovery by various methods of treatment:

No.	Form of treatment.	Cured.		Not cured.		Died.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.
404	Leube . . . . .	291	72	97	24	16	4
117	Lenhartz . . . . .	78	66	34	29	5	5
153	Nitrate of silver . . . . .	73	47	80	53	Ambulatory cases.	
110	Subnitrate of bismuth . . . . .	56	50	54	49	Ambulatory cases.	
10	Olive oil . . . . .	4	40	6	60	Ambulatory cases.	

**END RESULTS.** Of the 291 cases treated by the Leube method and cured, 83 could be followed for a period of five years or longer after the treatment. Of these, 62 or 74 per cent. remained permanently well, and 21 or 25 per cent. had relapses.

Of the 78 treated by the Lenhartz treatment, and cured, 45 could be followed for a period of five years or longer after the treatment. Of these, 35 or 77 per cent. remained permanently well, while 10 or 22 per cent. had relapses.

**RESULTS OF SURGICAL TREATMENT.** Of the 91 cases operated on, 64 or 71 per cent. were cured, 20 or 22 per cent. were not cured, and 7 or 70 per cent. died. Of these 10 had perforations, of which 6 or 60 per cent. recovered, while 4 or 40 per cent. died.

**END RESULTS.** Of the 64 cases operated on, and cured, 45 could be followed for a period of five years or longer, after treatment. Of these, 41 or 91 per cent. remained permanently well, and 4, or 9 per cent. had relapses.

**EINHORN DUODENAL FEEDING.** A few cases of ulcer which did not yield to the usual treatment were treated by Einhorn's duodenal method of feeding. While the results seemed satisfactory, the number of cases was too few to be incorporated in this report.

**CONCLUSIONS.** From a careful study of the 1000 cases of ulcers of the stomach and duodenum, the following conclusions may be safely drawn.

1. In patients suffering from various gastric disturbances, 7.8 per cent. are affected with ulcers.

2. The largest proportion of ulcers occur between the twentieth and fiftieth year of age.

3. More than twice as many males are affected as females.

4. Anemia is present in a large proportion of the cases of ulcer.

5. A history of over-indulgence in food or drink can be obtained in almost half of the number of cases of ulcer.

6. The greatest proportion of cases of ulcer presents a normal acidity, *i. e.*, 46 per cent.; 30 per cent. a hyperacidity, and 23 per cent. a subacidity. Hyperacidity is proportionately more frequently observed in males and subacidity in females. In recent ulcers and especially those accompanied by recent hemorrhage, the acidity is very high, while in chronic forms the acidity is low.

7. The average duration of symptoms is twelve years.

8. The most prominent symptom of ulcer, pain, occurs in 94 per cent. of cases, and pain is most frequent in cases associated with a high acidity. Pain appears sometimes immediately after

the taking of food (gastric ulcer), and at times long after the taking of food (duodenal ulcer). In many instances there are one or more periods of intermission of pain as well as the other symptoms; these periods vary from one to many months.

9. An epigastric tender area is present in at least 90 per cent. of all cases, a dorsal tender area in 32 per cent.

10. Vomiting is a very prominent symptom occurring in 67 per cent. of cases.

11. Hematemesis is present in 22 per cent. of cases and melena in 51 per cent. Melena is more than twice as frequent as gastric hemorrhage. Occult blood is present in 81 per cent. of the cases.

12. Of the 1000 cases of ulcer, 52 per cent. are duodenal and 40 per cent. gastric; the largest proportion occurring in males (58 per cent.).

13. Of the duodenal ulcers, 48 per cent. present normal acidity, 35 per cent. hyperacidity, and 16 per cent. a subacidity; hyperacidity being more frequently observed in males and subacidity in females.

14. Pain is present in 96.5 per cent. of duodenal ulcers, and is most prominent in cases with hyperacidity.

15. Distinct periods of intermission from pain and other symptoms, varying from one to twelve months or more, are exceedingly common in this affection.

16. Epigastric tenderness is present in 89 per cent. of the duodenal cases; a tender area to the right or left of the median line in 7 per cent.

17. Vomiting occurs in 21 per cent. of duodenal cases, and is more frequent in those accompanied by high acidity.

18. Melena occurs in 54 per cent. of duodenal cases, and occult blood is found in the stools in 83 per cent.

19. Seventy-two per cent. of cases of peptic ulcers treated by the Leube treatment are cured, 66 per cent. by the Lenhartz, 47 per cent. by the ambulatory treatment administering nitrate of silver, 50 per cent. with subnitrate of bismuth, and 40 per cent. with olive oil. Of the cases treated by the Leube cure, 74 per cent. remained permanently well, while 77 per cent. of those treated by the Lenhartz cure, likewise remained permanently well.

20. Seventy-one per cent. of the cases operated on are cured, 91 per cent. remaining permanently well.

The diagnosis of ulcer is often most difficult. The diagnosis of typical cases is not difficult, but the atypical forms form a great proportion of cases, and great difficulty is often experienced in drawing conclusions concerning such cases. Some of the important symptoms, such as pain and epigastric tenderness as well as nausea, vomiting, hematemesis, and melena, may be absent, or may be so overshadowed by other symptoms as to become insignificant.

The diagnosis of ulcer should never be made without the detec-

tion of occult blood in the stools, and yet when we remember that occult blood may appear in many other conditions, and that even in ulcer it often disappears, especially when the ulcer is healing, the difficulties in diagnosis become even greater.

The diagnosis between duodenal and gastric ulcer is often very difficult and many clinicians consider it is impossible in many instances to differentiate between the two. It is generally admitted that pain appearing two hours or more after meals (hunger pain), is indicative of ulcer of the duodenum, while pain appearing early is gastric. Hemorrhage is mainly observed in the vomitus in gastric ulcer, and most frequently in the feces in duodenal ulcer, but is often observed in both in either condition, and is of but slight importance in distinguishing the two forms, unless blood is persistently observed in the feces without being present in the gastric secretion.

Peptic ulcers are frequently mistaken for gastric neuroses associated with hyperacidity, and it is of the greatest importance to distinguish between these conditions.

Gall-bladder disturbances are to be differentiated from duodenal ulcers, but the diagnosis between the two conditions is often very difficult and sometimes impossible.

There can be no question but that a large proportion of ulcer cases recover under medical treatment. According to our observations, 72 per cent. by the Leube cure, 66 per cent. by the Lenhartz cure; this is in comparison to 71 per cent. treated surgically. When an ulcer patient is treated medically, he should be thoroughly treated, and ambulatory treatment should never be instituted. As we have shown, the results of ambulatory treatment are exceedingly unsatisfactory, inasmuch as in but from 40 to 50 per cent. of cases so treated is a cure effected. I believe that many ulcer cases do not recover because the treatment is not sufficiently prolonged. A rest cure of but a few weeks is often insufficient. In severe cases the patient should be put to bed for six or eight or even more weeks. The answer to the question whether the Leube or the Lenhartz treatment should be undertaken, depends largely upon the patient and the severity of the symptoms. Quite satisfactory results are often obtained by the Leube cure, and at times on account of the persistent nausea, vomiting, and pain, one is forced to follow this form of treatment. It is best when possible, however, to institute the Lenhartz treatment, for a restriction to liquid food is often unnecessary and usually results in great weakness and exhaustion. The anemia too frequently found accompanying this condition is often very extreme and the small quantities of milk which are consumed cannot prevent the onset of rapid exhaustion and emaciation.

Surgical intervention should only be considered if medical treatment has been persisted in for a sufficiently long period of time,



and has not been found effectual; especially is it indicated in those cases accompanied by severe and persistent pain, vomiting, or hemorrhage, or in ulcers recurring, notwithstanding thorough medical cure. The operation is indicated too in all pyloric or duodenal ulcers accompanied by stenosis. In ulcers situated at other parts of the stomach operation gives but slight relief unless radical procedures (resection or excision) are undertaken. Operation should be promptly practised in all cases of perforation.

---

## DIARRHEA OF GASTRIC ORIGIN: DIAGNOSIS AND TREATMENT.<sup>1</sup>

BY DOUGLAS VANDERHOOF, A.M., M.D.,

CONSULTING PHYSICIAN TO THE JOHNSTON-WILLIS SANATORIUM AND ATTENDING PHYSICIAN  
TO THE MEMORIAL HOSPITAL, RICHMOND, VA.

IN the study of gastro-intestinal disorders, chronic diarrhea is commonly classed among the conditions the cause of which may be obscure and the treatment, therefore, symptomatic and unsatisfactory. Diarrhea is a symptom and not a disease, and is to be regarded as the expression of a motor reaction of the intestines to irritants. The number and character of the irritant substances are many and varied—chemical, vegetable, and animal—while a purely functional diarrhea may occasionally ensue from an irritated nervous mechanism. Whatever the nature of the irritant in diarrhea, its action results in the production of a pathological acceleration of intestinal peristalsis. This increased peristalsis, in the majority of cases, is associated with some structural lesion in the walls of the intestine, but it may occur without such change. Furthermore, a diarrhea which owes its origin to the mere presence of irritants in the bowel contents may later be perpetuated by the development of definite anatomical changes in the intestinal mucosa. Such is probably the case in the form of diarrhea under discussion. It is the purpose of this article to direct attention to the clinical features of a not infrequent variety of diarrhea, the recognition of which should be simple in most cases, while the results of treatment are often brilliantly successful.

Diarrhea of gastric origin is dependent upon a condition of the stomach which may be either primary or in the nature of a reflex gastric disorder; most commonly a condition of anacidity, occasionally insufficiency of the pylorus, and rarely hyperchlorhydria. In the first two groups the food passes into the intestine insuffi-

<sup>1</sup> Read before the Johns Hopkins Medical Society, Baltimore, March 18, 1912.

ciently prepared by the usual gastric digestion and so acts directly as an irritant, or undergoes changes resulting in the production of irritant substances, while in cases of diarrhea associated with hyperacidity it is presumed that the entrance of the excessively acid secretion into the bowel is sufficient to set up increased peristalsis. The discussion in this article, however, is confined to the occurrence of diarrhea as a direct consequence of the failure of the stomach to produce its normal secretion of hydrochloric acid.

The term gastric anacidity is applied to those cases in which after an Ewald test breakfast there is no free hydrochloric acid and the total acidity does not exceed 20 "acidity per cent." It occurs in four groups of cases: (1) As a purely functional disturbance, either temporarily or over prolonged periods of time, with retained ferment secretions; (2) in achylia gastrica, a condition in which there is a permanent absence of all gastric secretions; (3) in pernicious anemia and certain metabolic disorders, as diabetes; and (4) in carcinoma of the stomach.

**INCIDENCE.** For purpose of analysis, I have made a statistical study of 500 patients in whom one or more gastric examinations were made. These cases are selected from my records of over 2000 private patients examined during the last four years in the course of general diagnosis work in internal medicine, not at all confined to diseases of the stomach. Gastric analyses were made only in cases presenting gastro-intestinal symptoms, or when such an examination seemed necessary to establish the diagnosis. For this reason the incidence of gastric anacidity to other lesions of the stomach cannot be exactly expressed. For example, cases of pernicious anemia that presented no difficulty in recognition were not necessarily submitted to gastric analysis, yet anacidity was undoubtedly present in every case. Of these 500 patients, 81, or 16.2 per cent., showed the condition of gastric anacidity. In a much larger series of 3147 patients, Kelling<sup>2</sup> reports 521 cases, or 16½ per cent. of anacidity. Of my 81 cases, 20 had cancer of the stomach, 22 were classified under the term neurosis, 5 were evident cases of chronic alcoholic gastritis, while the stomach findings in the remainder were associated with or regarded as reflex disturbances from the following conditions: Chronic appendicitis, 7 cases; cardiovascular disease and lesions of the female pelvic organs, each 4 cases; cholelithiasis, 3 cases; pernicious anemia, migraine, pellagra, pulmonary tuberculosis, and eyestrain, each 2 cases; and 1 case each of hysteria, peritoneal adhesions, benign tumor of stomach, myxedema, chronic influenza, and aural vertigo. One of the cases of chronic appendicitis was associated with definite hypothyroidism, and one of the pellagra cases was complicated with intestinal amebiasis. One patient, included above, had a

ruptured ectopic pregnancy and pelvic hematocele, and this was accompanied by severe attacks of gastric tetany, with pronounced dilatation of the stomach, ending in recovery.

Diarrhea was a prominent symptom in 13 of these 81 cases, including the 2 pellagra patients. Excluding these 2 cases, and the patients with malignant disease of the stomach, there were in the remaining 59 cases of gastric anacidity 11 patients with diarrhea, or approximately  $18\frac{1}{2}$  per cent. These 11 cases form the basis of this article, and most of them occurred in the group of patients in whom no organic cause could be ascertained as being responsible for the anacidity. A brief synopsis of the histories of these cases follows:

REPORT OF CASES. CASE I.—*Clinical summary: Matutinal diarrhea for two months; marked loss of weight and strength; no abdominal symptoms; complicating peripheral (toxic) neuritis; gastropnoxis; indicanuria; gastric anacidity on four examinations; prompt recovery from symptoms; gain of 46 pounds in two and one-half years, although condition of achylia persists.*

Mrs. B. (1030), aged fifty-four years. Date, September 20, 1908.

Complaint: Diarrhea and weakness.

Past history: General health good, 9-para. As a young woman was subject to attacks of "cholera morbus."

Present illness: Onset July 15, 1908, with loose bowels, and this condition has persisted ever since. Has lost 30 pounds; present weight 118. Has become distinctly weak, and fears she has either tuberculosis or malignant disease of the intestines. Has had no abdominal pain or cramps, but there has been a great deal of intestinal rumbling. The bowel movements occur for the most part in the early morning, generally number five or six, and then do not take place again until the following morning. The stools are always liquid, not particularly offensive, and have not contained any visible blood or mucus. Patient has had no fever, chills, or sweats. Appetite is poor, some nausea, no vomiting. No headaches. She is not a nervous woman. Several weeks ago she noticed that she was unable to flex the left foot when she put on her stocking, and now drags that foot slightly when walking. There is slight numbness below the left knee, but no pain in any of the extremities.

Examination: Complete physical examination of heart, lungs, deep reflexes, pupillary reactions, and glands is negative. Abdomen rather full and pendulous. The stomach on inflation is definitely enlarged and ptosed. No tenderness; no masses. Distinct weakness of anterior tibial group of muscles of left leg, with no sensory disturbances. Urine: The urine shows trace of albumin; indican much increased. Otherwise negative. Blood: Polymorphonuclear neutrophils, 45 per cent.; small mononuclears, 46 per cent.; large mononuclears and transitionals, 8 per cent.; eosinophils, 1 per

cent. No poikilocytosis; no nucleated red blood corpuscles; malarial parasites not present. Gastric analysis: Test breakfast removed in one hour; only a few cubic centimeters expressed. Free HCl, 0; lactic acid not present. Test breakfast repeated; removed in forty minutes; 85 c.c. obtained. Free HCl, 0; total acidity, 5; lactic acid not present.

December 17, 1908. Gastric analysis: Test breakfast, 20 c.c. removed in forty minutes. Free HCl not present.

January 8, 1909. Patient weighs 130½ pounds. For the last two months has had only one formed stool a day. Eats a general diet. No evidence of peripheral neuritis.

January 3, 1910. Patient weighs 153 pounds. Is perfectly well.

April 10, 1911. Patient weighs 164 pounds. Has never had any return of the diarrhea. Suffers more or less from vague pains about the larger joints. Urine continues to show great excess of indican.

December 30, 1911. Patient was requested to return for a gastric examination. This showed 60 c.c. expressed in forty-five minutes after an Ewald test breakfast. Clear, non-viscid fluid and coarsely divided bread particles; no visible blood or mucus. Free HCl, 0; total acidity, 6; lactic acid, 0; pepsin, 0; rennet ferment, 0. She says that she remains entirely free from any gastro-intestinal disturbances; bowels move once daily; stools almost always formed, and appear natural. Has had no nausea or flatulence. Has lost weight since last spring, and today weighs 152 pounds. Blood pressure, 182 mm. Hg.

CASE II.—*Clinical summary: Periodical attacks of diarrhea for years; on two occasions blood and mucus in stools. Recently tendency to loose bowels without actual diarrhea; no history of constipation; chief complaint is of indigestion, with symptoms of gastric hyperacidity; gastric anacidity on four examinations; complete recovery.*

Mrs. W. (1212), aged thirty-eight years. Date, January 29, 1909.

Complaint: Stomach trouble.

Past history: Operation for pelvic abscess five years ago. Prior to that no serious indigestion except occasional "bilious spells."

Present illness: Beginning seven years ago, patient has had irregular attacks of diarrhea, one of which lasted four months. On two occasions there was blood and mucus in the stools. For the last four months the bowels have had a tendency to be loose, without actual diarrhea. No history of constipation. Patient is subject to indigestion, characterized by pain occurring twenty minutes to half an hour after meals; it becomes worse during the next half hour, then gradually disappears. This pain is a sharp aching and burning, and is always intensified if patient eats acid fruits. Occasional nausea, no vomiting. No relief of pain by eating. Frequent abdominal distention and diffuse soreness.

Patient says that her symptoms are always worse when she is worried or nervous, while at other times she suffers very little from her stomach.

Examination: Heart, lungs, abdomen, superficial glands, and deep reflexes negative. Blood pressure, 110 mm. Urine, negative. Blood: Polymorphonuclear neutrophils, 75 per cent.; small mononuclears, 19 per cent.; large mononuclears and transitionals, 5 per cent.; eosinophiles, 1 per cent. Moderate anisocytosis; no nucleated red blood corpuscles; malarial parasites not present. Gastric analysis: Test breakfast removed in fifty minutes; 80 c.c. expressed. Free HCl, 0; total acidity, 4; lactic acid not present.

February 13. Gastric analysis: Test breakfast removed in forty-five minutes; 20 c.c. obtained. Free HCl not present.

March 10. Gastric analysis: Test breakfast removed in forty-five minutes; amount, 60 c.c. Free HCl, 0; lactic acid not present.

April 21. Gastric analysis (specimen sent by mail): Test breakfast, 5 c.c. submitted. Free HCl not present.

Patient remained under treatment for six weeks, then left for her home in West Virginia. It is interesting to note that the pain in the epigastrium entirely ceased while patient was taking 3 drams of dilute HCl daily. A letter received on May 24, 1909, says that she feels perfectly well, and that her weight has increased from 138 to 157 pounds. In July, 1910, patient called while in the city and said that she remained in the best of health. No further gastro-intestinal symptoms. A letter received from her on January 2, 1912, states that she continues to be entirely well.

CASE III.—*Clinical summary: Alternating diarrhea and constipation for three years, following severe attack of grip; bowels generally loose; matutinal diarrhea; no abdominal symptoms except flatulence; extreme weakness; stomach not enlarged or displaced; gastric anacidity; trichomonads in stools; good recovery.*

Mrs. T. (1335), aged sixty-three years. Date, April 26, 1909.

Complaint: Intestinal indigestion.

History: Patient says that she has never been very robust. Three years ago had four severe attacks of grip, and was ill the whole winter. Dates the onset of her bowel trouble to this illness. At times the bowels are constipated, but, as a general rule, are very loose. Frequently has eight or nine stools a day, which consist of nothing but water. Stools occur chiefly in the early morning. Has a good deal of gas in the bowels, but has suffered no abdominal pain. Has not lost weight, but has become extremely weak; can hardly walk. The diarrhea is always worse in the summer. Has had short periods of constipation, and on one occasion a fecal impaction, attributed to astringent medicine.

Examination: Poorly nourished woman. Skin dry. Complexion sallow, not cachectic. Blood pressure, 152 mm. Heart, lungs, deep reflexes, glandular system, pupillary reactions and rectum

negative. Blood: Polymorphonuclear neutrophiles, 51 per cent.; small mononuclears, 32 per cent.; large mononuclears and transitionals, 13 per cent.; eosinophiles, 4 per cent. Negative for malaria. Stool: Liquid; brownish green; moderate excess of mucus; no visible blood; many active trichomonads; no amebæ or other parasites. Gastric analysis: Test breakfast, 12 c.c.; expressed in one hour. Free HCl, 0; total acidity, 3; lactic acid not present.

Patient was treated in the hospital sixteen days and the bowels became constipated as soon as HCl was administered. She was seen at her home in a distant city about the last of December, 1909, and was last seen in April, 1911. Says that she remains perfectly well, eats heartily of general diet, and has had no return of the diarrhea.

CASE IV.—*Clinical summary: Patient says that her bowels are always "weak" and that she has "dysentery" every summer; much mucus in the stools, at times some blood; chief symptoms due to marked visceroptosis; gastric anacidity; improved under treatment.*

Mrs. C. (1450), aged thirty-nine years. Date, August 1, 1909.

Complaint: Pain in back, right side, and lower abdomen.

History: Patient says that her digestion is "quite good considering all she has the matter with her." Appetite good. Occasional attacks of "biliousness," associated with sick stomach and vomiting, but these only occur in the summer. Has had no sour stomach, no belching, but has a good deal of gas in her abdomen with rumbling. Suffers with "dysentery" every summer, but is not laid up with it. At these times has blood and mucus in the stools. Her principal complaint is of severe backache, pain in both flanks, and in the lower abdomen; feels as if everything would drop out of her when she stands. No history of cramp colic.

Examination: Heart, lungs, glandular system, and deep reflexes negative. Abdomen shows thin walls and visible peristalsis. The stomach on inflation much enlarged and displaced. The whole right kidney is easily felt. Slight diffuse abdominal tenderness, but no masses. Skiagraph after administration of bismuth shows that the pylorus lies just to the right of the navel; lesser curvature passes below the navel and upward on the left side parallel to the spine; the greater curvature reaches almost to the symphysis pubis. Gastric analysis: Test breakfast removed in one hour; 9 c.c. obtained. Free HCl, 0; total acidity, 6; lactic acid not present.

Patient was treated in the Johnston-Willis Hospital for six weeks. Distinctly improved. Adhesive straps applied to the abdomen which afforded much relief.

December 23, 1909. Patient has gained 20½ pounds; continues to wear adhesive straps to the abdomen; much improved in strength, with relief of abdominal symptoms.

CASE V.—*Clinical summary: Patient awakened early every morning by intestinal discomfort and rumbling, followed by loose stools; onset attributed to attack of grip two years ago. Appendectomy without relief of symptoms; no pronounced diarrhea, but stools never formed; gastric anacidity on five examinations; gradual recovery from symptoms, although the achylia persists.*

Mr. R. (1646), aged thirty-eight years. Date, January 14, 1910. Complaint: Discomfort in abdomen.

History: Patient had grip early in 1908, and his health has not been good since that time. Began to suffer with the bowel trouble of which he now complains. In October, 1908, the appendix was removed without amelioration of any of his symptoms. He had had one sharp attack of acute appendicitis three and one-half years before his operation. Patient complains chiefly of bad nights. Usually goes to sleep promptly, but is always awakened about 5 or 6 o'clock with a grumbling and uncomfortable feeling in the abdomen, especially over the bladder, which is always relieved by defecation. Complains very much of gurgling in the abdomen, and has a general peristaltic unrest. Has one or two stools before breakfast and one shortly after this meal. Stools are rarely formed, otherwise appear natural. Has passed no blood or mucus and has had no tenesmus. On rare occasions has short periods of constipation. Appetite quite good. No gastric symptoms. Complains of chronic fatigue and a variety of nervous symptoms. Average weight prior to appendectomy was 135 pounds; today he weighs 152 pounds.

Examination: Complete physical examination negative. Blood pressure, 146 mm. Stomach not displaced or enlarged. Urine negative. Gastric analysis: Test breakfast removed in forty-five minutes; 30 c.c. obtained. Free HCl, 0; total acidity, 3; lactic acid not present. Stool: Negative except for moderate number of fatty acid crystals. Blood: Polymorphonuclear neutrophils, 59 per cent.; small mononuclears, 31 per cent.; large mononuclears and transitionals, 9 per cent.; eosinophiles, 1 per cent. Negative for malaria.

April 7, 1910. Gastric analysis: Test breakfast removed in fifty minutes; 70 c.c. expressed. Free HCl, 0; lactic acid, not present.

June 1, 1910. Patient is definitely better but still has occasional attack of loose bowels in the early morning. Is discouraged about his condition.

Patient was sent to the Johns Hopkins Hospital, Baltimore, in July, 1910, and a letter from Dr. T. R. Boggs states that his findings correspond to those already mentioned and that the patient shows an absence of free HCl and very low total acid. It was noted that patient's tolerance for fat was somewhat low, although he took a free diet without fat loss.

March 10, 1911. Complete physical examination negative as before; weight, 134 pounds. Blood pressure, 155 mm. Urine, negative except for great increase of indican. Gastric analysis: Test breakfast removed in forty-five minutes; 140 c.c. expressed. Free HCl, 0; total acidity, 5; lactic acid not present. Patient is blue and depressed, but continues at his business. Bowels move once or twice early in the morning; stools generally formed. Continues to complain of gas and rumbling in the lower abdomen, which awakens him every morning at 3 or 4 o'clock.

December 18, 1911. At my request patient returned today for a stomach examination. He says that he is practically well, and has stopped worrying about himself now that he has learned to realize that his illness will not terminate fatally. Looks well; weighs 147 pounds. Has been taking 30 drops of the tincture of nux vomica before meals for two years, and HCl after meals for the same length of time. For the last eight months has substituted tablets of acidol with pepsin for the official HCl. Has absolutely no gastric symptoms. Bowels generally move once a day, and the stools are formed and appear natural. Occasionally has some aching "in the bowels" when he awakens in the morning, and at these times has some pain in the bladder. Has very little flatulence. Says that meat does not agree with him, but with the exception of this he eats a general diet and drinks buttermilk regularly. Blood pressure, 142 mm. Hg.

Gastric analysis: Test breakfast removed in forty-five minutes; 100 c.c. expressed. Free HCl, 0; total acidity, 2; lactic acid, 0; peptone, 0; pepsin, 0; rennet ferment, 0; erythrodextrin, 0.

CASE VI.—*Clinical summary: Persistent matutinal diarrhea for three years; gastric anacidity on three examinations; diarrhea ceased after administration of HCl with resulting constipation; trichomonads in feces; visceroptosis; arterial hypertension; continued nervous depression.*

Mrs. H. (1932), aged fifty-five years. Date, June 27, 1910.

Complaint: Diarrhea, weakness, and nervousness.

History: Patient has always been nervous. Suffered from a severe attack of nervous prostration twelve years ago. For the last three years has had a chronic diarrhea, characterized by four or five watery stools early each morning, with no actions during the rest of the day. Complains of frequent headaches, nervousness, and weakness. Appetite poor. Has lost considerable weight.

Examination: Enlarged heart, associated with mitral regurgitation. Blood pressure, 165 mm. Right kidney extremely movable. Area of gastric tympany increased and displaced downward; the greater curvature reaches  $2\frac{1}{2}$  inches below the umbilicus. Physical examination otherwise negative. Urine, negative. Indican not increased. Blood: Leukocytes, 5500. Negative for malaria. Differential count: Polymorphonuclear neutrophils, 64 per cent.;



small mononuclears, 16 per cent.; large mononuclears and transitionals, 11 per cent.; eosinophiles, 9 per cent. Stool shows undigested milk curds; small bits of mucus; no visible blood; many trichomonads present; no other parasites. Gastric analysis: Test breakfast removed in forty-five minutes; 30 c.c. obtained. Free HCl, 0; total acidity, 5; lactic acid present.

July 23. Gastric analysis: Test breakfast removed in fifty minutes; 5 c.c. expressed. Free HCl, 0; lactic acid not present. Patient's diarrhea, which had previously been but poorly controlled with bismuth, stopped immediately on the administration of HCl. Patient spent several months at Clifton Springs Sanitarium during the summer of 1910. Shortly after this she had several attacks, apparently crises of arterial hypertension, the blood pressure rising to 200 mm.

May, 1911. Patient remains obstinately constipated, continues in a depressed nervous condition. Blood pressure varies from 160 to 170. No gastric symptoms except flatulence.

CASE VII.—*Clinical summary: Periodical loose bowels for two years; diarrhea for one month; pronounced secondary anemia; mitral regurgitation; weakness; no loss of weight; no gastric disturbances; abdomen negative; gastric anacidity; diarrhea ceased promptly under treatment.*

Mrs. D. (2014), aged forty years. Date, October 18, 1910.

Complaint: Weakness and diarrhea.

History: Shortness of breath on exertion for fifteen years, quite pronounced recently. Moderate edema of ankles for four years. Appetite good. No gastric symptoms. For the last two years, short periods of diarrhea. No history of constipation. Onset of bowel trouble followed directly upon an attack of "typhomalarial fever." One month ago bowels became loose and have continued so ever since. Stools vary in appearance, usually watery; six to eight a day. Most of the bowel movements occur in the early morning, but also move in the afternoon. Patient has had some tenesmus, but has observed no blood or mucus in the stools.

Examination: Mucous membranes pale. Complexion, sallow; slight cyanosis. Marked pyorrhea. Blood pressure, 152 mm. Heart moderately enlarged. Mitral regurgitation. Lungs, negative. Spleen, palpable. Blood: Red blood corpuscles, 2,992,000; leukocytes, 6200; hemoglobin, 41 per cent. Differential count: Polymorphonuclear neutrophiles, 70 per cent.; small mononuclears, 14 per cent.; large mononuclears and transitionals, 13 per cent.; eosinophiles, 1 per cent.; mast cells, 2 per cent. Considerable anisocytosis; no poikilocytosis; no basophilic degeneration; no nucleated red blood corpuscles; malarial parasites not present. Urine, negative. Indican not increased. Stools were negative on two examinations. Gastric analysis: Test breakfast removed in

fifty minutes; 60 c.c. expressed. Free HCl, 0; total acidity, 3; lactic acid not present.

January 3, 1912. Patient was asked to return for observation but declined to have another gastric examination. She followed the treatment as outlined for about two months and the diarrhea ceased promptly and has not recurred. She says she is in much better health, but is still very anemic. Has no indigestion of any kind. Has gained 12 pounds in weight. Chief symptoms now referable to her anemia and heart lesion, but has had no further edema of the extremities. Blood: Red blood corpuscles, 3,568,000, leukocytes, 8600, hemoglobin, 43 per cent.. Differential count: Polymorphonuclear neutrophiles, 62 per cent.; small mononuclears, 25 per cent.; large mononuclears and transitionals, 11 per cent.; eosinophiles, 2 per cent. Red blood corpuscles show considerable variation in size and the majority of the cells are pale. No poikilocytosis, no basophilic degeneration, no nucleated red blood corpuscles. Malarial parasites not present.

CASE VIII.—*Clinical summary: Prolonged periods of matutinal diarrhea for four and one-half years; several times cured by administration of HCl; recurrences following acute illnesses; gastric anacidity on three examinations; at times mucus in stools associated with abdominal cramps; prompt recovery on treatment.*

Miss P. (2044), aged thirty years. Date, November 9, 1910. Complaint: Diarrhea.

Onset of present illness April, 1906, prior to which time she had been perfectly well. Contracted a severe case of measles complicated by bronchitis. Bowels became loose at that time. Patient consulted me in the fall of 1907 and two stomach examinations showed a condition of gastric anacidity which was thought to be responsible for her intestinal disturbance. Patient took HCl for three months and remained perfectly well for a year. Says that she was strong and fat. Then contracted bronchitis, followed by a return of the diarrhea. This has continued ever since at irregular intervals. Last fall patient was perfectly well for several months. Diarrhea began again in January of this year and lasted until March, returned in June. Patient has frequently been confined to her bed with it. The diarrhea always occurs early in the morning and forenoon; practically never has any bowel action after mid-day. Has had as many as fifteen stools a day, which were watery and yellow in color. She is always able to recognize any vegetable she may have eaten. At times has had considerable mucus in the stools and on these occasions suffers with griping pains which cease when the bowels move. No gastric disturbance except occasional nausea.

Examination: Complete physical examination negative. Patient is a well-developed woman. Stomach on inflation slightly enlarged but not ptosed. Blood: Polymorphonuclear neutrophiles,

54 per cent.; small mononuclears, 25 per cent.; large mononuclears and transitionals, 21 per cent. Negative for malaria. Urine, negative except for marked increase of indican. Gastric analysis: Test breakfast removed in forty-five minutes; 30 c.c. expressed. Free HCl, 0; total acidity, 9; lactic acid present. Stool shows numerous small flakes of mucus, but is negative for ova and parasites.

March 7, 1911. Patient called today while in the city to say that she remains perfectly well. Continued treatment until three weeks ago. Has gained 15 pounds in weight. Bowels are regular and she has one formed stool each morning.

CASE IX.—*Clinical summary: Moderate diarrhea for six months; preceding history of constipation; onset with fever; no abdominal pain or gastric symptoms; moderate anemia; weakness and loss of weight; gastric anacidity on two examinations; arteriosclerosis; pronounced improvement on treatment.*

Mr. P. (2101), aged sixty-one years. Date, December 16, 1910.

Complaint: Weakness and loose bowels.

History: No history of indigestion until six months ago. Last June had slight fever and began to suffer with loose bowels. Diarrhea continued until the middle of October, averaging two or three stools a day. Began to lose weight. Had no special indigestion. Then caught cold; became depressed; had some fever. Blood was examined, and was told he had malaria; took quinine. Has had no fever in the last three weeks. Says that his digestion and appetite are good, but he is afraid to eat because his bowels are loose.

Examination: Complete physical examination negative except that his blood pressure is 156 mm. with accentuation of the second aortic heart sound. Stomach slightly enlarged. Urine: Specific gravity, 1.014; albumin, distinct trace; indican, slightly increased; occasional hyaline and finely granular cast, otherwise negative. Blood: Hemoglobin, 76 per cent. Differential count: Polymorphonuclear neutrophiles, 72 per cent.; small mononuclears, 24 per cent.; large mononuclears and transitionals, 4 per cent.; eosinophiles, 0 per cent. Negative for malaria. Stool, negative for ova and parasites. Gastric analysis: Test breakfast removed in fifty minutes; 10 c.c. expressed. Free HCl not present.

April 21, 1911. Patient reports that his general condition is greatly improved. Has gained  $11\frac{1}{2}$  pounds in weight. Bowels move twice a day. Occasionally the actions are loose but whenever they are so he takes full doses of HCl and immediately they become formed again. Says he has no indigestion. His spirits are much better. Is greatly encouraged about himself. Blood pressure, 145 mm. Blood: Hemoglobin, 82 per cent. Differential count: Polymorphonuclear neutrophiles, 72 per cent.; small mononuclears, 22 per cent.; large mononuclears and transitionals, 6 per

cent.; eosinophiles, 0 per cent. Negative for malaria. Urine: Specific gravity, 1.022; albumin, faint trace; indican greatly increased; occasional hyaline cast. Gastric analysis: Test breakfast removed in forty minutes; 50 c.c. expressed. Free HCl, 0; total acidity, 18; lactic acid not present.

CASE X.—*Clinical summary: Patient awakened early in mornings with pain in her back and abdomen; matutinal diarrhea for several months, associated with flatulence; no gastric symptoms; gastric anacidity; complete recovery.*

Mrs. N. (2526), aged thirty-five years. Date, August 1, 1911.

Complaint: Pain in the back and abdomen.

History: No acute infections or serious illness until four and one-half years ago, when she had a severe attack of "erythema nodosum" when three months pregnant, which confined her to bed for seven weeks. Nine days after labor she had two chills and high fever, which persisted for two weeks. For five months after the birth of this child she suffered with symptoms similar to those of the present illness, but otherwise has been well, and bowels have always been regular. Onset of present illness was in March, 1911, after patient had been through a severe nervous strain nursing her sick mother. Began to suffer with a dead, aching pain in the small of the back radiating forward into the abdomen; never acute; not very noticeable during the day, and she rarely goes to bed with it. The pain generally awakens her about 4 or 5 o'clock in the morning. For the last few months her bowels have been loose, the first stool occurring about 5 A.M., and the bowels move again three or four times during the morning. The stools are large and watery, not offensive, and have contained no blood or mucus. Associated with this there has been a great deal of gas and rumbling in the abdomen which makes her nervous. On two or three occasions recently has been slightly nauseated; no other gastric symptoms. Appetite good, but patient has been dieting and her weight has diminished from 160 to 145.

Examination: Complete physical examination negative. Patient is a well-nourished and healthy looking woman. Blood pressure, 108 mm. No visceroptosis. Slight tenderness on deep pressure over the sigmoid and the head of the cecum. Blood: Polymorphonuclear neutrophils, 56 per cent.; small mononuclears, 31 per cent.; large mononuclears and transitionals, 11 per cent.; eosinophiles, 2 per cent. Negative for malaria. Urine, negative; indican not increased. Gastric analysis: Stomach found empty forty-five minutes after test breakfast. Test breakfast repeated; removed in thirty minutes; 40 c.c. expressed. Free HCl, 0; total acidity, 3; lactic acid present.

December 30, 1911. Patient reports from her home in North Carolina that she is perfectly well and fears she is getting too stout.

CASE XI.—*Clinical summary: Slight digestive disturbance for some years associated with constipation until three years ago; at that time had severe attack of biliary colic, with a second similar attack last summer; for the last three years persistent loose bowels in the early mornings; considerable flatulence; gastric anacidity on three examinations; operation showed chronic cholecystitis with one large gallstone and chronic appendicitis; recovery.*

Mrs. F. (2660), aged forty-four years. Date, November 6, 1911.

Complaint: Abdominal pain and indigestion.

History: At the time of the patient's marriage, eighteen years ago, she was thin and run down and had considerable indigestion for two years. Does not recall her symptoms, but had no abdominal pain, except one acute attack seventeen years ago, diagnosticated as appendicitis. No history of typhoid or other acute infections. Has complained of slight "indigestion" for years. Appetite good and regular; no nausea or vomiting, but has had considerable gas, which has caused bloating and pain. No pyrosis; no sour stomach or regurgitation of food. Bowels always constipated until the present illness. Onset of present illness three years ago, with severe attack of biliary colic. Her husband, a physician, says that ever since then she has had threatened attacks. A second severe attack occurred last summer. For the last three weeks the patient has suffered with a heavy aching in the epigastrium, coming two or three hours after eating. This has been relieved by induced vomiting, and the food has returned entirely undigested. For the last three years the bowels have been persistently loose, and at times watery, attributed in part to "cholelith pills," but also occurring independently of any cathartic medicine. Has averaged three or four stools a day; bowel movements almost invariably confined to early morning hours. Stools rather pale at present time; have contained no blood or mucus. No loss of weight. Two recent gastric analyses made by her husband have showed an anacidity without evidence of stasis.

Examination: Well-nourished woman; moderately anemic; no jaundice. Heart, lungs, pupillary reactions, deep reflexes, and glandular system normal. Blood pressure, 114 mm. Abdomen shows thick panniculus; stomach on inflation slightly enlarged but not ptosed. Decided tenderness on deep pressure overhead of cecum. Slight tenderness beneath the right costal border, but no gall-bladder block elicited. Urine: Distinct trace of albumin and great excess of indican; otherwise negative. Blood: Hemoglobin, 78 per cent. Differential count: Polymorphonuclear neutrophils, 60 per cent.; small mononuclears, 34 per cent.; large mononuclears and transitionals, 4 per cent.; eosinophiles, 2 per cent. Negative for malaria. Gastric analysis: Test breakfast removed in forty-five minutes; 100 c.c. expressed. Free HCl, 0; total acidity, 2; lactic acid present.

November 25, 1911. The diagnosis of chronic cholecystitis with probable chronic appendicitis having been made, patient was operated upon today at the Johnston-Willis Sanatorium. The appendix was thickened; had a club-shaped extremity, and was removed. The gall-bladder was greatly thickened and contracted with many adhesions about it. Contained about one ounce of pus, and one large solitary calculus was withdrawn from the cystic duct.

December 17, 1911. Patient was discharged well. Diarrhea began about a week after operation, but was controlled at once by administration of HCl.

The following case is reported because of its special interest, but is not included in the statistics for the reason that a gastric analysis was not obtained:

CASE XII.—*Clinical summary: Matutinal diarrhea of seven years' duration; onset following grip; trichomonads in stools but repeated examinations negative for other parasites; appendicostomy four years ago without relief; prolonged treatment with various intestinal antiseptics and restricted diet; gastric analysis not obtained; prompt recovery on administration of HCl.*

Mrs. K. (2179), aged fifty years. Date, January 19, 1911.

Complaint: Chronic diarrhea.

History: Seven years ago patient visited New Orleans. Shortly after this had an attack of grip, following which the bowels became loose and the diarrhea has continued ever since. She feared that she had contracted amebic dysentery in the South. Four years ago appendicostomy was done, although no amebæ had been demonstrated in the stools. Trichomonads were present on several examinations. Bowels irrigated through the appendix, with various solutions, without improving the intestinal condition, and after some months the wound was allowed to close. At present, the patient is on a limited diet. Says that she suffers from distressing intestinal peristalsis for an hour before rising in the morning. Generally has one stool before breakfast, and then has two or three stools after breakfast, generally goes to stool directly after lunch. The bowel movements are usually brown in color, loose or watery. Has passed considerable mucus at times. Patient suffers from soreness and a dragging in the bowels. No gastric symptoms.

Examination: Complete physical examination negative. Blood pressure, 154 mm. Spleen, palpable. Blood: Hemoglobin, 88 per cent. Differential count: Polymorphonuclear neutrophils, 64 per cent.; small mononuclears, 28 per cent.; large mononuclears and transitionals, 5 per cent.; eosinophiles, 2 per cent.; mast cells, 1 per cent. Negative for malaria. Urine: Specific gravity, 1.018; albumin, distinct trace; indican, much increased; occasional hyaline cast. Stools show considerable number of trichomonads,

but no other parasites. Gastric analysis was attempted and the stomach found empty when the tube was passed. Patient refused to take a second test breakfast.

Treatment was outlined on the supposition that the diarrhea was secondary to a gastric anacidity. In May, 1911, patient reported that she took HCl regularly for three weeks and at irregular intervals since. The diarrhea has entirely ceased. Has had no further intestinal disturbance to the present time.<sup>3</sup>

**SYMPTOMATOLOGY.** The gastro-intestinal symptoms associated with the condition of gastric anacidity vary considerably in different individuals. While most of these patients suffer with symptoms referable to the stomach, yet in a certain proportion the complaint is entirely confined to the state of the bowels, and in a still smaller number of patients gastric anacidity exists with absolutely no symptoms on the part of the gastro-intestinal tract. In this series of 81 cases of gastric anacidity there were several instances of very minor digestive disturbances. In 3 patients, however, there was no history whatever of symptoms referable either to the stomach or the bowels. One of these patients was a gentleman of splendid physique, aged forty-one years, whose only complaint was susceptibility to head colds; another patient was a young society matron who became run down after a season of gayety and feared she had contracted tuberculosis; and the third case was a business man, aged forty-four years, a hard worker, never taking vacations, who complained of being always tired and irritable.

In several studies on achylia gastrica by various authors, cases have been reported in which a complete lack of gastric secretion has persisted for many years without apparent detriment to the general health. Such patients may present no subjective symptoms whatever, can take any form of food without discomfort, and the small intestine assumes vicariously the function of the stomach. Friedenwald<sup>4</sup> mentions a case in which gastric anacidity had persisted for twelve years, with gain in weight, and with but few attacks of intestinal disturbance. He also quotes Ewald's case, in which there was absence of gastric secretion for two and one-half years, during which time the patient gained 42 pounds in weight. Case I in my series—a patient with achylia gastrica—increased 46 pounds in weight in two and one-half years. Einhorn<sup>5</sup> reports a similar case that was under observation for four years. Thus it is evident, as Einhorn has indicated, that patients with gastric anacidity may be divided into three groups,

<sup>3</sup> This patient was seen in June, 1912. She said that a gastric analysis made at the Johns Hopkins Hospital January, 1912, showed no free hydrochloric acid and an absence of pepsin and rennet ferment. Her diarrhea remains entirely controlled by the continuous use of small doses (10 drops) of dilute hydrochloric acid after meals, but recurs as soon as the acid is discontinued.

<sup>4</sup> Osler's Modern Medicine, v, 157, Lea & Febiger, 1908.

<sup>5</sup> Diseases of the Stomach, 1906, fourth edition, p. 375.

according to (1) absence of gastro-intestinal symptoms; (2) symptoms mainly gastric, and (3) symptoms chiefly intestinal.

In a series of 112 cases of anacidity studied by Friedenwald<sup>6</sup> there were 8 patients presenting no gastro-intestinal symptoms; 69 patients complaining of a greater or lesser variety of gastric symptoms; and 35 patients having apparently no gastric symptoms but presenting marked intestinal disturbances. Just what factor comes into play to bring on the diarrhea is not always evident, but it is of interest to note that in 6 of my cases the patients dated the onset of the diarrhea to some acute illness (Cases III, V, VII, VIII, IX, and XII).

**CLINICAL FEATURES.** The clinical features of diarrhea secondary to gastric anacidity are clear cut and definite in the majority of instances, so that not infrequently the diagnosis can be suspected before the stomach analysis is made. The leading symptoms may be enumerated as follows:

1. Diarrhea: The most striking feature of the diarrhea is its occurrence early in the morning and during the forenoon. As a rule it may be said that patients with this condition are unlikely to have any bowel movements in the afternoon or at night. This matutinal diarrhea often awakens the individual from sleep at 5 or 6 o'clock in the morning, a second call to stool generally occurs before breakfast, and one to three bowel movements take place between breakfast and the mid-day meal. In other patients the diarrhea is more profuse, with very frequent stools. Even so, the trouble is generally through for the day by the time luncheon is reached, as in Case VIII, with as many as fifteen stools a day. In some cases the diarrhea may alternate with constipation, but often the constipation may be attributed to full doses of astringent drugs, with which these patients are so often treated.

2. Character of the stools: The bowel movements are liquid and inoffensive, as a rule, and show the presence of macroscopic particles of undigested food, especially fruit and vegetables. In other cases the stools are soft and yellow, and show an excess of fatty acid crystals. Mucus and blood are not usually seen, but may occur during exacerbations of the symptoms. The presence of trichomonads was noted in 3 of my cases (III, VI, and XII).

3. Flatulence and peristaltic unrest is the rule, especially in the early morning hours. With this there may be griping pains throughout the abdomen, although most patients are free from actual abdominal pain. Irritability of the bladder, relieved after defecation, is not uncommon. This was so pronounced in Case V that the patient kept insisting that his kidneys must be diseased.

4. Gastric symptoms are often lacking or are overshadowed by the condition of the bowels. The entire absence of any com-

<sup>6</sup> Loc. cit.



plaint referred to the stomach is rather striking in this group of cases. The appetite is generally unimpaired, although the patient may be afraid to eat. Occasionally there is slight nausea, and, curiously enough, as in Case II, the patient may recite the symptoms of hyperchlorhydria.

5. Loss of weight and strength may develop quickly after the intestinal disturbance sets in. In other cases, with distinct weakness and prostration, there may be no diminution of the body weight. Early in the disease, and in the absence of complications, the patient does not look ill. Other individuals may show a marked secondary anemia, as in Case VII, but quite distinguishable from the blood picture of pernicious anemia.

6. Indicanuria is pronounced in most cases. Muscular pains and slight recurring arthritis are not uncommon, or there may be a definite neuritis, as in Case I. In the treatment of such cases the administration of hydrochloric acid has as specific an action as the salicylates in acute rheumatic fever.

7. Appearance of the test breakfast: In these cases of gastric anacidity the ingested food makes a relatively short stay in the stomach. This organ empties itself so quickly that often no remains of the Ewald test breakfast can be obtained after the lapse of one hour. This is easily accounted for by the absence of the normal "acid control" reflexly exerted over the pylorus by the first portion of the duodenum.<sup>7</sup> It is advisable to pass the stomach tube in forty or forty-five minutes after the breakfast has been taken. The material obtained shows a characteristic gross appearance. The bread particles are coarsely divided and show no evidence of having been acted upon by any digestive agent, and the fluid portion is clear, thin, and colorless, without visible blood or mucus. The usual tests for the presence of free HCl are negative, and the total acidity is usually below 10 "acidity per cent." Lactic acid, while generally absent, may be present in a distinct amount even in cases showing no evidence of stasis (Cases VI, VIII, X, and XI).

PROGNOSIS. The prognosis of diarrhea secondary to gastric anacidity depends very largely upon the condition of the bowel wall, and this in turn rests upon the duration and intensity of the accompanying bacterial infection. The regular and normal secretion of hydrochloric acid by the healthy stomach is classed by Herter<sup>8</sup> as one of the defensive actions of the body against bacterial invasion. When the hydrochloric acid secretion is deficient, not only does the ingested food pass into the intestines in coarse "undigested" particles, but it carries with it a host of accidental, saprophytic forms of bacterial life, which immediately come into contact with the "obligate" and well-adapted parasitic

<sup>7</sup> W. B. Cannon, *The Mechanical Factors of Digestion*, Chapter IX, *The Acid Control of the Pylorus*, New York, 1911.

<sup>8</sup> *The Common Bacterial Infections of the Digestive Tract*, 1907.

forms of the intestinal tract. Hence, regarded in a certain light, hydrochloric acid is our best intestinal antiseptic. In his work on the infections of the digestive tract, Dr. Herter has shown that the absence of free hydrochloric acid is a feature of nearly all cases of pronounced saccharo-butyric putrefaction. He also believes that in all such cases the mucous membranes of the digestive tract are almost constantly in a state of excessive irritation, so that stimuli which in normal people would meet with little response give rise to excessive peristalsis and diarrhea. Thus, very clearly, a vicious circle is established.

W. Soltau Fenwick refers to the vicarious action of the intestines in the light of a compensatory adjustment, which is effective over a greater or lesser length of time and then is followed by a characteristic train of symptoms when this process of compensation begins to show signs of failing. The course of events is well expressed in his own words:<sup>9</sup> "In cases of diminished gastric acidity, peptic digestion is seriously interfered with, but a much larger proportion of starch is converted into sugar, and the work of the intestine in this respect is lessened. Although this condition is attended by a corresponding diminution in the amount of bile and pancreatic juice, compensation remains complete, owing to the fact that less alkali is required for neutralization and consequently a greater proportion remains available for the digestion of proteids and fats. The intestinal secretions also vary both in quantity and quality, with the composition of each meal; an excess of starch or proteids being productive of increased amylolytic or tryptic activity, while a diet composed largely of fat chiefly stimulates the secretion of bile and steapsin. These automatic adjustments may continue to work with perfect precision for a considerable time, but sooner or later the functions of the small intestine and other digestive glands become exhausted, and the processes of compensation begin to exhibit signs of failure. Under these circumstances fat is usually the first constituent of the food to suffer, and its diminished absorption is evidenced by an increased evacuation of neutral fats and combined fatty acids. Subsequently the proteids undergo excessive putrefaction and finally, the carbohydrates are decomposed by bacterial action and the production of sugar is arrested. This failure of compensation naturally occurs at an earlier date when the gastric disorder arises from organic disease. Thus, when subacidity ensues from chronic gastritis the intestine becomes hampered not only by the products of abnormal fermentation, but also by the presence of bacteria, and consequently intestinal inflammation, accompanied, perhaps by an infection of the biliary or pancreatic ducts, almost invariably develops and seriously interferes with the functions of digestion.

<sup>9</sup> W. S. Fenwick, *Dyspepsia; Its Varieties and Treatment*, 1910, p. 415.

In like manner, a continuous and excessive hyperacidity of the gastric juice tends to exhaust the activity of the pancreas and to excite a form of chronic intestinal inflammation which eventually arrests the solution and absorption of food."

**TREATMENT.** The essential point in the treatment of patients with the condition of gastric anacidity is the administration of large amounts of hydrochloric acid. The usual dose of 10 or 15 drops of the official dilute hydrochloric acid is inefficient. In these cases hydrochloric acid is not to be regarded as a drug. Its administration is for the sole purpose of supplying artificially a substance which the normal stomach secretes regularly and in good quantity. Not only is this acid indispensable for the activation of pepsinogen into pepsin, but on reaching the duodenum it serves as a hormone, or chemical messenger, to initiate the flow of pancreatic secretions.<sup>10</sup> Furthermore, hydrochloric acid may be regarded in a certain sense, as the most effective intestinal antiseptic, as I have already indicated. The only obstacle presented in the use of this acid is the difficulty of giving it to our patients in sufficient amounts. The mucous membranes of the throat will tolerate only weak solutions, hence the necessity of much fluid as a diluent. It is my custom, however, to prescribe 30 drops of the official dilute hydrochloric acid in a full glass of water one-half hour after meals, to be repeated again in one-half hour, or a total of 180 drops per day. On occasions, during the last year, I have substituted for the mineral acid, tablets of acidol. This is an ingenious synthetic product, hydrochloride of betain, a substance derived from molasses in the manufacture of beet sugar. When dissolved in water, or in the stomach, acidol gradually liberates hydrochloric acid. The only objection to the preparation is its cost, but it is much more palatable and convenient to carry about than the liquid acid.

In the effort to stimulate the glands of the stomach to resume their function the most efficient means at our disposal are the administration of strong meat broths as the first course of the meal, preceded by full doses of tincture of *nux vomica*. This drug should be pushed to its physiological limits and patients may often take 30 or 35 drops at the dose. It might be argued that *nux vomica* may give rise to a gastric hyperesthesia, or aggravate such a condition if it already exists. The studies of Steele,<sup>11</sup> confirming the previous experience of Musser, show, however, that *nux vomica* in full doses does not have such an effect, but relieves rather than increases the tendency to hyperesthesia of the gastric mucous membranes.

In addition to the drinking of broths, *consomme*, *bouillon*,

<sup>10</sup> E. H. Starling, *Recent Advances in the Physiology of Digestion*, Chicago, 1907, p. 85 et seq.

<sup>11</sup> The Relation of Excessive Gastric Acidity to Gastric Symptoms, *Jour. Amer. Med. Assoc.*, 1906, xlvii, 496.

beef tea, etc., these patients are encouraged to have their foods well salted, in order that the chlorine supply of the body be ample for the production of hydrochloric acid. If any restriction of the dietary is indicated, undoubtedly the proteids should be the class of foodstuffs to limit in amount. With diminished peptic digestion, associated with a possibly impaired tryptic activity, proteids are certainly not well handled, and their excess in the intestine permits of undue decomposition with the production of increased amounts of indol and other cleavage products which we believe to be injurious to the organism.

Buttermilk is a specially valuable article of diet in cases of gastric anacidity, and most patients can be induced to consume three pints a day. When they tire of it, or if it is not well borne, one of the various preparations of lactic acid bacillus tablets may be given.

If the general nutrition is much impaired, associated, as is usually the case, with visceroptosis and possibly motor insufficiency of the stomach, the patient will be much benefited by assuming the recumbent position for an hour after each meal, or may be instructed to lie on the right side. Further treatment may include the wearing of an abdominal supporter, and the employment of the usual measures to combat anemia, nervous states, and other conditions which may be not only the result, but as well the contributing cause of a gastric anacidity.

---

**MULTIPLE SUBCUTANEOUS HEMANGIOMAS, TOGETHER  
WITH MULTIPLE LIPOMAS, OCCURRING IN ENORMOUS  
NUMBERS IN AN OTHERWISE HEALTHY, MUSCULAR  
SUBJECT.**

BY JOHN T. BOWEN, M.D.,

EDWARD WIGGLESWORTH PROFESSOR OF DERMATOLOGY, *Emeritus*, HARVARD UNIVERSITY.

THE patient was a man, aged thirty-six years, a native of Russia, who had been in this country twenty-six years. His family history was irreproachable. His father and mother were alive and well; he had four brothers who were healthy, and all of the family were living in America. None of the family had had any skin disease. He was married and had one healthy child.

He was first seen in March, 1910. He was of small stature, but exceedingly muscular. During the early part of his life and until eight years previously he had been a professional boxer of considerable reputation, and had had matches in various parts of the world. He had never sustained any serious injury. His weight

was 147 pounds. He said that he had first noticed his present affection three or four years previously, after he had given up his sporting career, and had engaged in his present occupation, that of a builder. The first lesions to make their appearance were on the back, one or two in number, and they had steadily multiplied since.

The lesions were numerous, small or moderate-sized tumors, most of them subcutaneous, so that the skin was freely movable over them. In a few instances there seemed to be a slight involvement of the corium. The surface of the skin was normal, with the exception that in a few places, not necessarily over the tumors, there was a bluish-red color from venous stasis. The distribution of these nodules and tumors was over the trunk especially. The thighs were affected, although much less prominently, and there were only a few lesions on the upper and lower arms. The head and face were completely free, and there were very few lesions upon the neck. In size the lesions varied from that of a small pea to a pigeon's egg. They were moderately firm and elastic. They were either rounded or elongated in shape, and those of medium size could in many instances be picked up between the fingers, and gave the feeling of disks or coins. The lesions were absolutely non-sensitive.

The patient was seen again nine months later, in November, 1910. The nodules had increased considerably in numbers. Some of the larger ones were now the size of a hen's egg, and their outlines could be faintly seen when the patient was examined at a distance of a few feet. A photograph of the patient would have shown only these few slight protuberances, which represented the larger lesions, the hundreds of smaller lesions which studded the trunk being subcutaneous and invisible. The patient preserved his appearance of magnificent muscular development without apparently any excess of fat tissue. The patient was positive that none of the nodules had disappeared, and he was equally certain that new ones in large numbers had appeared since last seen nine months before. There was no glandular enlargement to be detected then or at any other time. No nodules had appeared upon the head or trunk, with the exception of the tongue. During the last six months a nodule had appeared on the tip of the tongue, and it had attained the size of a bean. It was sharply elevated, only slightly excoriated, firm to the touch, and had annoyed him somewhat in eating and drinking, although it was not specially sensitive. There were no signs or symptoms in the throat. The lesion of the tongue was excised and the wound healed quickly.

The case was again examined and studied in October, 1911, and in March, 1912. The lesion of the tongue that has just been described had not reappeared and there were no abnormal appearances of the head and face. The tumors, however, especially those

FIG. 1



FIG. 2

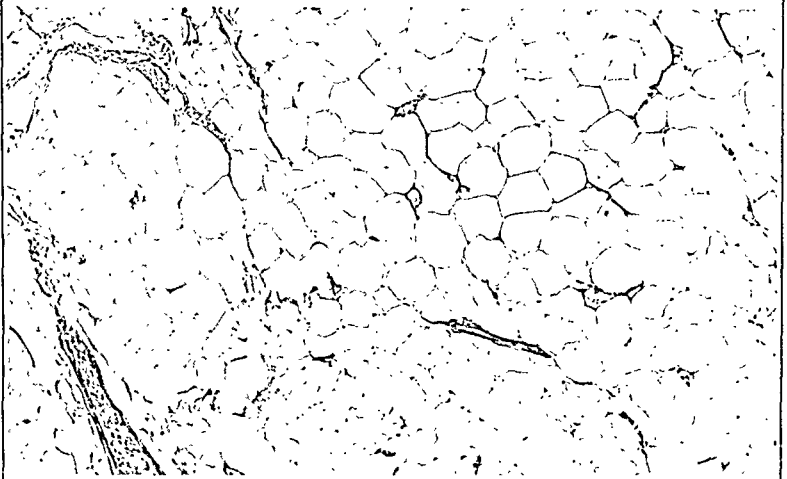


FIG. 3



FIG. 1.—Section from one of the smaller nodules, showing growth of bloodvessel-infiltrating the fat tissue.

FIG. 2.—Section from one of the larger nodules, showing pure fat tissue.

FIG. 3.—Section from the lesion of the tongue, showing a pure hemangioma.



upon the trunk, had increased greatly in numbers, and there were certain ones of larger size than before. In most places there was barely an interval of half an inch in which tumors could not be felt. Some of the larger ones, especially those upon the back and loins, had reached the size of a hen's egg, and in a few instances there were ill-defined masses, although, as a rule, the tumors were sharply bounded. The protrusion of some of the larger tumors was somewhat more pronounced, so that the appearances were slightly more evident to the eye. A few purpuric patches were present, sometimes over the lesions, sometimes not. None could be felt over the buttock, where, as indeed everywhere, he was very muscular. The largest tumor was situated on the back over the left scapular region. This tumor was somewhat elongated and less sharply defined than the majority. No lesions could be detected on the head or face, nor on the hands or feet. The thighs were moderately involved, and there were a few nodules on the lower arms and lower legs. There were no lesions on the genitals.

A careful internal examination at this time was made by Dr. J. H. Pratt, but nothing abnormal could be detected. Examination of the secretions showed no deviation from health. The patient's general health was perfect and the only symptom produced by these multitudinous growths was mental disquietude as to the final outcome.

**HISTOLOGICAL EXAMINATION.** Several of the lesions of varying sizes were excised for microscopic examination. The lesions in most instances "shelled out" readily after incision of the overlying skin, and presented microscopically a yellowish appearance, similar to that of lipomas. They were resilient to the feel. Microscopically a difference was in general to be noted between the smaller or more recent, and the larger tumors. The smaller tumors, of which Fig. 1 offers a good example, were composed of a new-growth of bloodvessels, which seemed to be infiltrating the fatty tissue in every direction within the limits of the tumor. No distinct capsule could be detected, but the tumor was sharply bounded from the normal tissue surrounding it, as was evidenced by the ease with which it was expressed after incision. In the larger nodules the amount of new-formed angiomatous tissue became much less in comparison with the fatty tissue. This gradation was very marked and constant in all the lesions excised, some half dozen in number, of varying sizes and duration of growth. The larger tumors were composed almost entirely of fatty tissue (Fig. 2), and the only difference that they exhibited from ordinary lipomas was that they might be considered somewhat more vascular. Mitotic figures were occasionally to be found in the newgrowth of bloodvessels. None could be seen in the fat tissue, but that was to be expected, considering the difficulty of such findings in ordinary lipomas.



The lesion of the tongue was totally excised. This proved to be a pure hemangioma, as shown in Fig. 3, with no fat apparent. Mitotic figures were seen in the proliferating vascular branches.

In the search of the literature that has thus far been possible no precisely similar instance has been discovered. The pronounced complication, with what must be regarded as fat hyperplasia, might call to mind the numerous cases of multiple symmetrical lipomas that have been reported from various sources in various countries. In none of these that I have seen described were the clinical appearances at all like those of the case in question. The cases of multiple lipoma present usually large masses of fat tissue in places, so that it is difficult to speak of them simply as tumors. No instance of such an extraordinary number of small tumors has been discovered among these multiple lipomas. I find a reference to an article by Berenbruch,<sup>1</sup> describing a peculiar case of multiple angiolipoma, but I have not been able to see the original. A remarkable case is described by Winternitz and Boggs,<sup>2</sup> in which there were multiple subcutaneous hemangio-endotheliomas; also the same of the intestinal tract, multiple polypi of the stomach undergoing malignant change, generalized vascular sclerosis, and cirrhosis of the liver in a mulatto, aged sixty-five years. The writers say that they could find in the literature no similar instance of multiple subcutaneous hemangio-endotheliomas. In this case the subcutaneous tumors presented a cavernous aspect.

The tendency of angiomas to infiltrate the fat tissue is well known (Borst, Ribbert). In many of these cases the growth of vessels is at the expense of the fat tissue, which gradually disappears.

In the case reported the fact that in the smaller and younger lesions the hemangiomatous element was most pronounced and that there was a gradual and progressive increase in the amount of fat tissue as the lesions became more developed, would favor the view that the growth of vessels is the primary process. The appearance of a single pure hemangioma upon the tongue where the fat tissue is normally scanty is also in accord with this theory. It seems as if the angiomatous growth invading the fat tissue causes an increase of this tissue, which in time overshadows and dominates the vascular growth, so that the larger tumors are indistinguishable from true lipomas.

<sup>1</sup> Ein Fall von Multiplen Angio-Lipomen combinirt mit einem Angiom des Rücken-markes, Tübingen, 1890.

<sup>2</sup> Johns Hopkins Hospital Bulletin, July, 1910.

MALIGNANT DISEASE OF THE LUNG WITH SPECIAL  
REFERENCE TO SARCOMA.<sup>1</sup>

By A. A. STEVENS, M.D.,

PROFESSOR OF THERAPEUTICS AND CLINICAL MEDICINE, WOMAN'S MEDICAL COLLEGE OF PENNSYLVANIA; LECTURER IN MEDICINE, UNIVERSITY OF PENNSYLVANIA, ETC.

SECONDARY malignant disease of the lung or pleura is not uncommon. It may arise by metastasis from distant organs or by direct extension from adjacent structures. Secondary cancer of the lung may be associated with an initial focus in one of the abdominal viscera, as the liver or pancreas; but in a larger percentage of cases it results from the extension of a primary mammary, esophageal, or thyroid carcinoma. Encephaloid or medullary cancer is the form that most frequently reaches the lung by metastasis. Secondary sarcoma of the lung most commonly originates in a primary growth in the marrow cavity of one of the long bones. The small round-cell form is most often noted.

Two autonomous formations approaching closely to both carcinoma and sarcoma in their morphological characteristics, and appearing in many cases as secondary growths in the lungs are the so-called hypernephroma and the malignant deciduoma. Of 22 cases of hypernephroma collected from the literature by Woolley<sup>2</sup> there were metastasis in the lungs in 13. Although the primary growth in these cases may correspond morphologically to carcinoma or adenocarcinoma, it not rarely affords metastasis of a purely round or small spindle cell sarcomatous type. Rolleston and Marks,<sup>3</sup> Woolley,<sup>4</sup> Adami,<sup>5</sup> and others emphasize this point. Malignant deciduoma, which genealogically is more closely related to carcinoma than to sarcoma, involves the lungs secondarily in nearly 50 per cent. of the cases, and in some instances is first manifested by coughing, pleuritic pain, hemoptysis, and other symptoms referable to the chest.

Primary carcinoma of the lung is rare. In the records of the Breslau Pathological Institute, out of 9246 necropsies, in which there were 1000 cases of malignant disease, Pässler,<sup>6</sup> found 16 cases of primary carcinoma and 4 cases of primary sarcoma of the lung. Seydel<sup>7</sup> among 10,829 autopsies made at the Munich Pathologic Institute found records of 1342 tumors, and of these 184, or 13.7 per cent., were in the lungs or pleura. In 83.2 per cent. the tumors were metastatic and in 16.8 per cent. the tumors were primary. Of

<sup>1</sup> Read before the Section on General Medicine of the College of Physicians of Philadelphia), March 25, 1912.

<sup>2</sup> AMER. JOUR. MED. SCI., cxxv, 1903.

<sup>4</sup> Loc. cit.

<sup>6</sup> Virchow's Arch., 1896, Band cxiv, S. 191.

<sup>3</sup> Ibid., cxvi, 1898.

<sup>5</sup> Principles of Pathology, i, 747.

<sup>7</sup> Münch. med. Woch., 1910, lvii, No. 9.

the primary growths 11 were sarcoma of the pleura and 20 were carcinoma of the lung.

With other observers primary carcinoma has been more rare and primary sarcoma more common than the statistics indicate. Reinhard<sup>8</sup> found only 5 cases of primary carcinoma in 8716 necropsies. Rolleston and Trevor<sup>9</sup> in analyzing the post-mortem records of St. George's Hospital from January 1, 1890, to July 8, 1902, comprising 3983 cases, discovered only 8 cases of primary malignant disease of the lungs. Of these, 3 were primary sarcoma of the lung, 2 were primary sarcoma of the bronchi, and 2 were primary carcinoma of the bronchi. There was no case of primary carcinoma of the lung itself. The apparent inconsistencies in the statistics may be attributed in part to differences in nomenclature and in part also, without doubt, to the fact that some of the older writers incorrectly classified their cases. Indeed, as Mallory's<sup>10</sup> studies have shown, it may be very difficult or even impossible to make definite statements in regard to the cellular structure of many tumors without operative removal and immediate tissue fixation.

Primary sarcoma of the lung may spring from the lymphatic glands surrounding the bronchi, especially those in the roots of the lung, from the lymphatic vessels themselves, or from the subpleural or intrapulmonary connective tissue. Tumors developing within the lung from the connective tissue are most frequently of the spindle-cell variety, whereas those originating in the lymphatic vessels are commonly of the nature of endothelioma. Endothelioma of the pleura often invades the lung, and unless the growth is studied histologically in its entirety it may readily be mistaken for lymphosarcoma or carcinoma. As a rule, primary sarcoma is limited to one lung. It forms a large infiltrating mass, of variable consistence, and of a grayish color, often mottled with hemorrhagic areas. Metastasis, except to the mediastinal glands and tissues, are not common. In the 8 cases of primary sarcoma of the lung itself studied by Rolleston and Trevor,<sup>11</sup> remote metastasis were noted but once. In primary cancer, on the other hand, secondary growths are found with great frequency in the various abdominal organs, and not rarely in the muscles.<sup>12</sup>

The dominant symptoms of malignant disease of the lung may be those of a progressive consolidation of the lung, of stenosis of the larger bronchi or trachea, or of pleurisy with effusion. Cough and dyspnea are rarely absent. The cough varies in severity and quality, according to the size and location of the growth. It is especially marked when the larger bronchi are involved or the

<sup>8</sup> Quoted by Villanene, *Russkij Wratsch*, October 30, 1904.

<sup>9</sup> *Brit. Med. Jour.*, February 14, 1903.

<sup>10</sup> *Jour. Med. Research*, 1905, viii, 113.

<sup>11</sup> *Loc. cit.*

<sup>12</sup> Menetrier, *Art. Neoplasie*, Bouchard's *Patholog. Gen.*, vol. ii; Handford, *Trans. Path. Soc.*, London, 1888, xxxix, 48.

mediastinum is invaded and the trachea compressed. In the latter event the cough is likely to be paroxysmal and of a ringing quality, as in aneurysm of the thoracic aorta. On the other hand, when the tumor is confined almost entirely to the vesicular structure the cough may be very slight. There is also much variation in the degree of dyspnea. When the trachea is compressed, or a large pleural effusion present, it may be intense and for a considerable period the only obtrusive symptom. Expectoration occurs in a large proportion of cases, but it may be slight or even absent. Stokes laid much stress upon the occurrence of a gelatinous reddish (currant-jelly) or brownish-black (prune-juice) sputum, evidently the result of the intimate admixture of mucus and blood; but sputum of this character also occurs in other pulmonary conditions. Occasionally, disintegration of the tumor gives rise to copious fetid expectoration resembling that of gangrene. In a number of instances the diagnosis has been made certain by the microscopic examination of tissue fragments in the sputum.

Hemoptysis, from congestion of the tissues surrounding the tumor, or erosion of fair-sized pulmonary vessels, is present in the majority of cases, and may be profuse and persistent. Pain is inconstant. It is often quite severe, however, when the pleura is involved or the thoracic nerves are compressed. Recurring attacks of pleuritic pain are not rarely the first symptom to attract attention. Enlargement of the superficial veins of the chest and localized edema sometimes result from invasion of the anterior mediastinum and occlusion of large venous trunks. More rarely, hoarseness and dysphagia arise from pressure upon the recurrent laryngeal nerve and esophagus respectively. Enlargement of the glands above the clavicle or in the arm-pit is an important symptom, but it is quite exceptional in sarcomatous cases. The temperature remains, as a rule, normal, but not infrequently in the later stages moderate fever of a remittant type supervenes and persists until the end. Cachexia sooner or later develops in most cases, and is of importance in differentiating tumor from aneurysm.

In the absence of pleural effusion, percussion usually reveals an irregular area of dullness, gradually increasing in extent. If the bronchi in the affected region are pervious, auscultation elicits bronchial breathing and broncophony. In the majority of cases, however, the bronchi are occluded, and, in consequence, both respiratory sounds and voice sounds are feeble or suppressed. When the root of the lung is involved and a main bronchus partially obstructed the respiratory sounds over a limited area may be loud and stridulous. The chest wall over the tumor is sometimes distended, but it may be retracted if there are extensive pleuritic adhesions. In tumors attaining large dimensions the heart and abdominal organs are often considerably displaced. In a case of sar-

coma of the thorax cited by Rolleston<sup>13</sup> the liver was so depressed that its lower border was on a level with the umbilicus.

In a large percentage of cases, symptoms of pleurisy with effusion dominate the clinical picture. If the fluid is not bloody at first, it usually becomes so after two or three tapplings. Microscopic examination of the sediment sometimes affords valuable diagnostic aid. A large number of cells exhibiting numerous mitoses, especially asymmetrical division forms is in favor of malignancy (Rieder, Warthin, Dock). Rarely, secondary nodules have developed along the course of the aspiration wound.

The following cases illustrate the important features of sarcoma of the lung:

CASE I.—W. P., a male, aged twenty-four years, with a good family history. His habits had been regular and he denied venereal infection. He did not recall having had any of the ordinary diseases of childhood, with the exception of diphtheria at the age of six. After that illness he enjoyed unbroken good health until about four months before admission to the hospital, January 12, when following exposure he was seized with sharp pain in the right side of the chest. His family physician treated him for pleurisy, and in four weeks his symptoms entirely disappeared. He remained in the "best of health" until six weeks before entering the hospital. At that time he developed what seemed to be a severe cold. The symptoms were those of sore throat, with hoarseness, hacking cough, and the expectoration of frothy mucus. This condition continued unchanged for about three weeks, when he noticed one morning on arising that his face was swollen, especially over the right cheek. The swelling subsided during the day, but returned each morning. Subsequently the neck and right side of the chest also became swollen. He had slight dyspnea, but no pain, and his appetite and digestion were good. On admission the patient's condition was as follows: The face, neck, and right side of the chest were markedly edematous. The skin was pale, but the appearance was not cachectic. The tongue was slightly coated, pale, and flabby. The voice was husky; beyond slight congestion of the vocal cords, however, there was nothing abnormal in the larynx. There was slight cough at intervals, with the occasional expectoration of frothy mucus. The pupils were equal and reacted well both to light and accommodation. The eye-grounds, except for slight congestion of the retinal vessels, were normal.

The right side of the chest was nearly 4 cm. larger than the left at the level of the nipples. Respiratory movements were absent on the right side and the intercostal spaces were obliterated. The apex beat was in the sixth interspace, near the anterior axillary line, and was forcible. Vocal fremitus was entirely absent over the

right side, both anteriorly and posteriorly. On percussion there was flatness over the entire right side, except anteriorly above the clavicle. The cardiac dullness extended in the fifth interspace about 5 cm. to the left of the midclavicular line. On the left side there was hyperresonance. No respiratory sounds could be detected on the right side, except near the sternoclavicular articulation, where the breathing was bronchial. There were no friction sounds or rales on the right side, and vocal resonance was extremely feeble. On the left side the breath sounds were much exaggerated and scattered moist rales could be heard. A soft systolic murmur was audible at the apex of the heart, and was not transmitted. The heart sounds at the aortic area were normal. The pulmonary second sound was somewhat accentuated. The liver dullness merged above into the thoracic flatness and extended below about 5 cm. below the costal border in the midclavicular line, otherwise nothing abnormal was found in the abdomen. Neither on admission nor at any other time could enlargement of the glands in the axilla or above the clavicles be detected. The respirations were 24 to 28, and not labored; the temperature ranged between 99° and 100°; the pulses in the radial arteries were synchronous, but that on the right side was distinctly weaker than that on the left; the urine contained a trace of albumin, but no casts. Examination of the blood revealed: Hemoglobin, 65 per cent.; red blood cells, 3,872,000; white blood cells, 13,400.

January 13. The right pleural cavity was tapped at two points: first, about 3 cm. below the angle of the scapula, and then 6 cm. below the angle of the scapula, near the posterior axillary line. Each puncture brought away about 50 c.c. of bloody fluid, which soon coagulated. Much resistance was offered to the entrance of the needle, and unless the direction of the cannula was frequently changed the flow of blood would cease. The clinical diagnosis was intrathoracic growth, probably sarcomatous.

January 15. The patient's condition was not materially changed.

January 16. The physical signs were unchanged. The patient stated that his appetite was good, that he had slept well, and was very comfortable. A blood examination revealed 15,600 leukocytes, of which 68.5 per cent. were polymorphonuclears, 29 per cent. were lymphocytes, 2 per cent. were large mononuclears, and 0.5 per cent. were eosinophiles.

January 17. The patient, against orders, got up and went to the toilet at the end of the ward. Returning he fell across the bed in a state of collapse, and died within a few minutes.

*Autopsy.* Body of a well-nourished man; skin and mucous membranes pale; rigor mortis (ten hours) well marked. Heart much displaced to left side. Left pleural sac was without adhesions and free from fluid. The left lung was somewhat congested and edematous, but otherwise normal. In the right pleural sac there

were dense adhesions, with loculi containing bloody serum, the latter amounting in all to about 120 c.c. The right lung was large and firm. It weighed 2500 grams. On section it was found to be infiltrated throughout, except for a small portion of the lowest lobe posteriorly, with a dense mass of purplish gray color. A few areas of softening about the size of a pea were noted. No tuberculous foci were present. Neither the peribronchial nor the mediastinal glands were enlarged. The pericardium contained a few cubic centimeters of straw-colored fluid, and was without adhesions. The heart was slightly dilated and relaxed. It weighed 320 grams. The valves were normal. The abdominal cavity contained about 300 c.c. of clear fluid. The liver was slightly adherent to the diaphragm. It weighed 1450 grams. It was congested and apparently somewhat fatty. The spleen was congested and firm. The other abdominal organs presented no gross changes. No secondary nodules were discovered. Microscopic examination of the growth revealed a typical spindle-cell sarcoma.

CASE II.—A. C., aged thirty-four years, a clerk by occupation, with a good family history. He always enjoyed good health until seven months before he came under observation, when he developed pain under his left scapula. This was shortly followed by a cough, with mucous expectoration and occasional attacks of hemoptysis. The blood was bright red in color. He sought advice in a medical dispensary and was treated for tuberculosis, but did not improve. On the contrary, his cough grew worse, his expectoration became mucopurulent and profuse, the pain continued, he developed night sweats and often felt feverish, and in three or four months lost twenty pounds.

On admission the patient weighed 118 pounds, and presented a somewhat cachectic appearance. The chest was long and flat. The left side was immobile and slightly depressed. There was no glandular enlargement. The apex beat of the heart was invisible. Tactile fremitus was marked on the right side and absent on the left side, except anteriorly above the fourth rib and posteriorly above the scapular spine. On percussion there was flatness on the left side of the chest, extending from the fifth rib anteriorly to the fourth rib in the midaxillary line, and the spine of the scapula posteriorly. Over the right lung there was hyper-resonance. On auscultation scattered dry and moist rales were heard over the right side of the chest and over the upper lobe of the left lung. On the entire right side and over the left side below the clavicle there was harsh, vesicular breathing. Over the flat area on the left side the breath sounds were scarcely audible. Examination of the heart revealed no abnormalities. The organ was apparently not displaced. The abdomen was slightly distended, but otherwise showed no changes. The temperature ranged between 97.5° F. in the morning and between 100° and 101.5° F. in the evening. The pulse was 90

to 110; the respirations were usually 24 to 30; the urine was free from albumin, casts, and sugar. An examination of the blood showed: Hemoglobin, 70 per cent.; red blood cells, 3,440,000; white blood cells, 12,400. The sputum on repeated examinations failed to show tubercle bacilli. The left pleural sac was punctured on three occasions, with negative results.

During the next four weeks there was no decided change in the general symptoms, although the patient became distinctly weaker and more emaciated. The expectoration was often blood-streaked, but only once in this period was there any marked hemoptysis. Dyspnea, which was slight at first, was now evident, especially on exertion. The fever and sweats continued as before, but there were no chills. Another examination of the blood, and the last one made, showed: Hemoglobin, 65 per cent.; red blood cells, 3,200,000; white blood cells, 14,600.

In the fifth week, during a severe paroxysm of cough, he brought up in the sputum two particles of solid matter, one about the size of a small cherry-stone, the other somewhat smaller. They were of a grayish-pink color, irregularly rounded, and firm. Upon microscopic examination these particles were found to be made up of a close aggregation of large round or slightly oval cells. The cytoplasm was abundant and the nuclei were deeply staining. There was very little interstitial reticulum. A diagnosis of intrathoracic sarcoma was now made. Three days after the expectoration of the fragments the patient was attacked with severe hemoptysis, which continued intermittently for about six hours. Following this he was much exhausted. Four days later he had another copious hemorrhage, followed by collapse, from which he never rallied. Death occurred about eight months after the appearance of the first symptom.

*Autopsy.* The body was much emaciated; the pleura on the left side presented firm adhesions below and posteriorly. On the right side there were slight adhesions posteriorly. Both pleural cavities contained a small quantity (50 c.c.) of bloody serum. The left leaf of the diaphragm was enormously thickened and tightly adherent to the left lung and spleen. The aorta, heart, and diaphragm were firmly united by adhesions. The bronchial, mediastinal, and abdominal glands were all much enlarged, but firm. The right lung was congested and edematous. On section the left lung, except at the apex, was found to be studded throughout with numerous pinkish-white nodules, varying in size from that of a pea to that of an egg. Most of these were firm, but two or three of the larger ones were almost gruel-like in consistence. The right lung was congested and edematous. It contained no nodules. The heart, apart from the adhesions surrounding it, showed no abnormalities. The peritoneal cavity contained no excess of fluid, but presented local adhesions in the neighborhood of the diaphragm, spleen, and left kidney. The right adrenal body was about the size of a small



egg, and completely replaced by a soft, reddish-white growth. The latter also extended a short distance into the superior pole of the left kidney. The right kidney, stomach, pancreas, liver, and intestines were apparently normal. No other nodules were discovered. The brain was not examined.

Microscopically the nodules in the lung presented for the most part the same picture as the fragments found in the sputum during life, although in places the resemblance to sarcoma of the alveolar type was close.

Microscopic examination of the adrenal growth showed it to be a so-called hypernephroma, some areas presenting a typically adenocarcinomatous aspect, and others exhibiting just as definitely the characters of alveolar sarcoma.

CASE III.—G. A., a Greek, aged thirty-six years, a laborer by occupation. Owing to the lack of an efficient interpretation only an imperfect history could be obtained. He had been sick for several weeks, complaining of pain in the right side of the chest, dyspnea, and cough without expectoration. During the six days that he was under observation these symptoms were still present. He was a man of medium height, decidedly pale, but not markedly emaciated. Dyspnea was very pronounced, and his lips and finger-tips were blue. The temperature throughout was normal or subnormal; the respirations were between 24 and 36; the pulse ranged between 110 and 120; the urine was somewhat scanty, but otherwise not abnormal. An examination of the blood showed: Hemoglobin, 60 per cent., red blood cells, 3,260,000; white blood cells 12,000. The physical signs were those of a pleuritic effusion on the right side. This side of the chest was immobile and appeared to be slightly distended, although the interspaces were not obliterated. Fremitus was absent and the percussion note was flat at all points below the clavicle in front and the spine of the scapula posteriorly. The breath sounds were inaudible. Over the left side of the chest there were a few scattered coarse rales, but otherwise only the usual evidences of compensatory action. The apex beat was diffuse in the fifth interspace, and slightly to the left of the midclavicular line. There were no murmurs. The lower border of the liver could be felt below the costal margin, but apart from this the results of the abdominal examination were negative. Two punctures of the right pleural sac were made on different occasions; the first yielded a few cubic centimeters of serum faintly tinged with blood, and the second, about 80 c.c. of fluid decidedly hemorrhagic. The clinical diagnosis was pleurisy with effusion, probably tuberculous. Two days after the last aspiration pulmonary edema suddenly set in and terminated fatally.

*Autopsy.* At the autopsy only the thoracic findings were of interest. The right pleural cavity contained about half a liter of bloody serous fluid. The pleural surfaces were firmly adherent over the uppermost lobe, both anteriorly and posteriorly. Below

there were no adhesions except over the diaphragm. The pleura throughout was enormously thickened and covered with numerous cartilaginous nodules. The right lung was compressed, hyperemic, and edematous. In the middle lobe there were two yellowish-white nodules, having a diameter of about 3 cm.; in the lowest lobe there were a number of nodules ranging in size from a millet seed to a hazelnut. The left pleural cavity was empty, and the left lung was hyperemic and edematous. The heart was pale and flabby, but otherwise not abnormal. The enlargement of the intrathoracic lymph glands could be detected.

Microscopically, sections of the pleura showed numerous anastomosing tubules lined with one or two layers of cubical epithelial cells, and separated by a rather dense network of connective tissue. Interspersing the latter were many round cells, with abundant cytoplasm, and deeply staining nuclei, somewhat like those in round-cell sarcoma. Microscopic examination of the nodules found in the lung revealed a wide-meshed net of delicate connective tissue, the meshes of which were filled with large round cells, having an epithelioid appearance. The cells were packed tightly in the acini, and were in immediate contact with the reticulum as in alveolar sarcoma. Many vessels were seen in the trabeculae. The anatomical diagnosis was endothelioma of the right pleura with metastasis in the right lung.

The diagnosis of pulmonary malignant disease is often a matter of great difficulty, only to be arrived at by a careful collation of all the facts and a close observation of the progress of the case. Pulmonary tuberculosis, pleural effusion, or aneurysm, is usually suspected. Not rarely the symptoms throughout are so indefinite that the true nature of the condition may only be determined post mortem. The discovery of malignant disease elsewhere, of course, furnishes an important clue. This clue is likely to fail, however, when the growth is sarcoma and is primary in the lung. Even when the pulmonary affection is secondary the symptoms of the metastatic tumor may overshadow the entire clinical picture and the primary focus escape recognition, as in one of the cases cited above. Occasionally the examination of scraps of tissue found in the sputum furnishes conclusive evidence. In this way the diagnosis was established in Case II. Wolff,<sup>14</sup> Claisse,<sup>15</sup> Ehrlich,<sup>16</sup> Betshart,<sup>17</sup> Feldt,<sup>18</sup> Demorest<sup>19</sup> and Cornil<sup>20</sup> also cite instances in which the microscopic examination of tissue fragments from the sputum afforded decisive information. When pleural effusion is present, the character of the fluid, its rapid return after thoracentesis, and the cytological findings are sometimes suggestive. However, too much importance should not be attached to the occurrence of a slightly bloody exudate, since

<sup>14</sup> Fortsch. d. Med., Nos. 18 and 19, 1895.

<sup>15</sup> Lancet, March 11, 1899, p. 712.

<sup>16</sup> Quoted by Hampeln, Zeit. f. klin. Med., 1897, Band xxxii, H. 3 and 4.

<sup>17</sup> Virchow's Arch., Band cxliii, H. 1.

<sup>18</sup> Deutsch, med. Woch., 1903, xxix, No. 28.

<sup>19</sup> Med. Rec., January 16, 1904.

<sup>20</sup> Comp. rend. de Soc. Anat., January 27, 1905.

this is not uncommon in tuberculosis and pleurisy complicating chronic nephritis and other wasting diseases. In cases marked by consolidation of the lung, suspicion may be aroused by certain anomalies in the clinical picture, as the unusual location or distribution of the dull areas and the constant presence of blood in the sputum without tubercle bacilli. The fact must not be forgotten, however, that tuberculosis and malignant disease of the lungs not rarely coexist. Tuberculosis was present in 13 of 31 cases of malignant disease of the lung reported by Wolff<sup>21</sup> and in 3 of 10 cases reported by Schwalbe.<sup>22</sup> Hildebrand,<sup>23</sup> Seigert,<sup>24</sup> Ribbert<sup>25</sup> and Menetrier<sup>26</sup> also cite cases in which tuberculosis and malignant disease were associated in the same lung.

In any case much importance is to be attached to symptoms pointing to stenosis of the air passages, although in tumors developing within the lung these do not appear, as a rule, until the disease is far advanced, and even when such symptoms are well marked the existence of aneurysm must often be debated.

Pulmonary syphiloma may produce signs closely resembling tuberculosis on the one hand or malignant disease on the other. In the absence of any positive evidence of tuberculosis or malignant disease, a positive Wassermann reaction should be regarded as an indication for recourse to specific treatment. Echinococcic disease of the lung and dermoid cyst may yield most of the symptoms of malignant growth, although both are even more rare than the latter. Of 1816 cases of echinococcic disease occurring in the United States and collected by Sommer<sup>27</sup> the lung or pleura was involved in 147. Apart from the presence of cysts elsewhere, the expectoration of hydatid membrane, and the data afforded by thoracentesis, there are no characteristic signs. Presumptive evidence, however, might be forthcoming in the presence of pronounced eosinophilia and the fixation of complement in the hemolytic test. Exploratory puncture is not without danger, owing to the grave toxemia which may follow absorption of the hydatid fluid. Maydl<sup>28</sup> reports 11 cases of intrathoracic echinococcus disease in which a fatal result followed thoracentesis.

In the case of intrathoracic dermoid cyst the coughing up of hair is the only pathognomonic symptom. According to Shaw and Williams<sup>29</sup> this was observed in 7 of the 35 authentic cases reported in the literature up to 1905.

Except in rare cases the treatment of tumors of the lung or pleura can only be palliative. In the 31 cases analyzed by Seydel there were only 7 in which an operation would have offered the slightest chance of recovery.

<sup>21</sup> Loc. cit.

<sup>22</sup> Deutsch. med. Woch., 1896, xii.

<sup>23</sup> Virchow's Arch., 1893, Band cxxiv.

<sup>24</sup> Gaz. Heb. de Méd. et de Chirurg., 1899, No. 6.

<sup>25</sup> New York Med. Jour., August 22, 1896.

<sup>26</sup> Ueber Echinokokkus der Pleura, Wien, 1891.

<sup>27</sup> Ziegler's Beiträge, 1888, Band ii.

<sup>28</sup> Deutsch. med. Woch., 1896, xi.

<sup>29</sup> Lancet, November 4, 1905.

## PAROXYSMAL HEMOGLOBINURIA.

BY ROBERT A. COOKE, M.D.,

NEW YORK.

(From the Department of Experimental Therapeutics and the Department of Practical Therapeutics, Cornell University Medical College, New York City.)

As a clinical entity, paroxysmal hemoglobinuria was first recognized and described by Dressler in 1854. In spite of the many clinical studies and the amount of experimental work on isolated cases, however, no satisfactory hypothesis was advanced to explain the pathology of this rare and curious disease until 1904, when Donath and Landsteiner<sup>1</sup> contributed their first paper to the subject. They attributed the attack characteristic of the disease to a specific hemolyzing substance in the blood of these patients, and they demonstrated its presence by experiments *in vitro*. Eason<sup>2</sup> working independently, had found this same hemolyzing substance in a case under his care. Since then a number of observations have been made by different investigators, all of whom confirm the presence of the autolysin; but with regard to the definite mode of action of this substance on red blood corpuscles there is even now no unanimity of opinion. The case here reported was studied with a view to clearing up, if possible, some of the disputed points.

**HISTORY.** E. P., aged thirty-eight years, porter, colored, single, was admitted to the hospital November 10, 1911.

*Family History.* Father, four brothers, and four sisters dead; cause unknown. Mother and one sister living and well. The sister resides in New York City and, so far as known, has never had an attack of hemoglobinuria.

*Personal History.* Patient was born in the West Indies, where he lived until eleven years ago, when he came to New York City. His habits are good; alcohol and tobacco in moderation.

*Previous History.* An indefinite history of a short, mild attack, called malaria, once before coming to New York. Venereal disease denied, and no symptoms elicited suggesting an acquired infection.

*Present History.* Nine years ago, having been in New York City two years, the patient had an attack which came on suddenly in November, 1902, while he was working and apparently in excellent health. This attack consisted of a severe shaking chill, with fever, followed by the passing of black urine. In twelve hours he was as well as usual, and the urine looked normal. One week later he had a similar experience. Beginning one month later, January, 1903, he had attacks in rapid succession, and was in a hospital for ten

<sup>1</sup> Münch. med. Woch., 1904, li, 1590; Zeit. f. klin. Med., 1906, lviii, 173.

<sup>2</sup> Edinburgh Med. Jour., 1906, xix, 43; Jour. Path. and Bact., 1906-7, xi, 167.

weeks, without improvement, the paroxysms continuing at intervals throughout the summer and up to September, 1903, when they ceased spontaneously, and he was perfectly well for two years. Since September, 1905, the paroxysms have recurred at irregular intervals, for the most part in the cold season, but occasionally in summer. He found that washing his hands in cold water would induce an attack, and he says the summer attacks always followed chilling in a draught after hard work. All of the attacks since January, 1903, have been associated with severe, sharp, lancinating pain in the lumbar region, especially the right. There is also numbness and tingling of the extremities, which subsides with the attack.

*Physical Examination.* The patient is a well-built, rather small negro. He is absolutely normal, with the exception that on abdominal examination a smooth rounded mass is found in the upper quadrant on each side, taken to be the kidney, moderately enlarged, slightly movable, and not tender.

Cystoscopy: December 19, 1911, by Dr. E. L. Keyes, Jr. Bladder normal, mouths of the ureters normal, bloody urine from both ureters.

Radiograph: "Does not show calculus in either urinary tract."

Urine Examination: During an interval the urine is clear, of normal specific gravity, with no albumin. An occasional cast is found, but no pus cells and no red blood cells. During an attack the urine is dark reddish brown, containing much coagulable proteid, few leukocytes, and an occasional red blood cell. Chemical test for blood, positive.

Blood Examination: Without special reference to the attacks the blood shows: Leukocytes, 4400 to 7200; polymorphonuclears, 62 per cent. to 65 per cent.; hemoglobin (Dare), 62 per cent. to 65 per cent. (November to December, 1911), 72 per cent. (March 16, 1912).

Red blood cells, 2,700,000 (November 29, 1911), 3,600,000 (February 14, 1912), 4,800,000 (March 16, 1912). Coagulation time, eight to nine minutes (normal). Blood plates, 500,000. Malarial parasites, absent.

Wassermann Reaction: Positive, December 4, 1911.

Salvarsan: 0.5 gm., given intravenously, February 19, 1912.

Wassermann Reaction: Positive, March 25, 1912 (by Dr. L'Esperance).

Salvarsan: 0.4 gm., given intravenously, April 7, 1912.

Wassermann Reaction: Positive, April 15, 1912 (by Dr. Noguchi).

Luetin Test: Positive April 15, 1912 (by Dr. Noguchi).

Salvarsan: 0.6 gm., given intravenously, April 29, 1912.

Wasserman Reaction: Positive, May 30, 1912.

On January 5, 1912, the Ehrlich experiment was done. A tourniquet was placed about the left arm above the elbow, and the fore-

arm was immersed in ice water for five minutes. The arm was then taken out and dried, and blood was drawn from a finger into a test-tube containing a small amount of 0.8 per cent. NaCl solution. This was warmed and centrifuged. Hemolysis was present. As a control, blood was taken from a finger on the right hand, which was not immersed, before the tourniquet was removed from the left arm. This was also put in a test-tube containing a small amount of salt solution and warmed. Hemolysis was absent. During the immersion the patient complained of intense lumbar pain, with tingling of all the extremities. Within a half hour after the experiment the patient had a severe shaking chill, with rise of temperature to 102° F. The first urine voided was dark reddish brown. Urine voided three hours later was also dark brown, but the urine voided six hours after the experiment was perfectly clear amber colored.

We have then to do with a perfectly typical case of paroxysmal hemoglobinuria in a man without history and with none of the stigmata of congenital or acquired syphilis, but with a positive Wassermann reaction and positive luetin test.

The particular point of interest in this pathological condition is the hemolysin, which will be considered under the following headings: (1) Demonstration of the autohemolysin; (2) absorption of the auto-antibody from inactive serum; (3) dissociation of corpuscle antibody combination; (4) absorption of complement from active serum; (5) action of complement on red blood cells sensitized with inactive hemolytic serum; (6) mode of action of the autohemolysin; (7) etiology of paroxysmal hemoglobinuria.

The preparations used in the work here reported are designated as follows: (1) "P. Ser." The serum of the hemoglobinuric patient obtained by centrifuging defibrinated blood while still warm. (2) "P. Ex. Ser." Defibrinated blood of the same case was subjected to 0° C. for one hour, then centrifuged quickly in the cold and the serum removed. (3) "P. Ina. Ser." Some of the serum obtained in (1) was inactivated at 55° C. for twenty minutes. (4) "N. H. S." Normal human serum obtained from defibrinated blood. (5) "N. Ex. Ser." Defibrinated blood, same as (4), at 0° C. for one hour, centrifuged quickly in the cold and the serum removed. (6) "G. P. Ser." Guinea-pig serum from defibrinated blood. (7) 10 per cent. "P. Blood." From the hemoglobinuric case. (8) 10 per cent. "N. H. Blood." Normal human blood from the same case as the serum in (4). (9) 10 per cent. sensitized sheep's blood.

For these suspensions (7 to 9) 5 c.c. of the defibrinated blood were washed three times with 0.8 per cent. warm NaCl solution and made to 50 c.c., with 0.8 per cent. NaCl solution. All preparations were freshly made on the day in which the experiments were done. In every instance at least seven days had intervened since an attack. These experiments are confirmatory of a number of earlier experiments carried out on this case, in which hemolysis was shown, not only for his own but other human corpuscles. In incubating for

hemolysis it was found that after icing, if the tubes were warmed over a free flame carefully, one-half hour in the incubator was sufficient for maximum hemolysis. This technique was employed in all my cold-warm experiments.

1. DEMONSTRATION OF THE AUTOHEMOLYSIN. By subjecting oxalated blood of a hemoglobinuric patient or the serum and a corpuscle suspension of the same blood to a low temperature, then incubating at 37° C., Donath and Landsteiner obtained hemolysis "in vitro." No hemolysis took place on prolonged exposure to the cold only nor on prolonged incubation at 37° C. only. This so-called "cold-warm" experiment has given positive results in the hands of all other observers, although Meyer and Emmerich<sup>3</sup> were successful only thirty times in a total of sixty-nine experiments on four patients, and Kumagai and Inoue<sup>4</sup> were compelled to modify the original technique to get satisfactory results. In the twelve separate times that the case here reported was examined, positive results were always obtained by the original Donath-Landsteiner method.

TABLE I.—Demonstration of Autohemolysin.

A.			Lysis.
0.200 cc P. Ser. + 0.25 cc 10% P. Blood	0° C. ½ hr.		Nearly complete
0.100 cc P. Ser. + 0.25 cc 10% P. Blood	Warmed		Partial
0.050 cc P. Ser. + 0.25 cc 10% P. Blood	37° C. ½ hr.		Slight
0.025 cc P. Ser. + 0.25 cc 10% P. Blood			0
Control: 0.2 cc P. Ser. + 0.25 cc 10% P. Blood	37° C. 1 hr.		0
Control: 0.2 cc P. Ser. + 0.25 cc 10% P. Blood	0° C. 1 hr.		0
B.			Lysis.
0.2000 cc P. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood			Complete
0.1000 cc P. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.		Nearly complete
0.0500 cc P. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed		Strong
0.0250 cc P. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.		Trace
0.0125 cc P. Ser. + 0.3 cc N. H. S. + 0.25 cc 10 %P. Blood			0
C.			Lysis.
0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C.	0	Warmed
0.3 cc N. H. S. + 0.25 cc 10% N. H. Blood	1 hr.	0	37° C. ½ hr.

To demonstrate the autolysin, the experiments given in Table I were done. The results obtained show the characteristic hemolytic action with the "cold-warm" experiment, while the controls, that is, icing alone and incubating alone, are negative. Comparison of A with B shows a deficiency of complement in the "P. Ser." to completely activate all the antibody present, for the addition of complement by "N. H. S." in B shows a smaller complete lytic dose than in A and establishes 0.2 c.c. as the minimum complete lytic dose of the "P. Ser." for the amount of corpuscles used, in the presence of sufficient complement. C shows the absence of auto-

<sup>3</sup> Deut. Arch. f. klin. Med., 1909, xevi, 287.

<sup>4</sup> Deut. med. Woch., 1912, No. 8, p. 361.

lysin in "N. H. S." and the absence of an isolysin for "P. Blood," and this serum can therefore be used as complement.

2. ABSORPTION OF ANTIBODY FROM INACTIVE SERUM. Donath and Landsteiner, and Eason also, in their first papers demonstrated the hemolysin concerned in paroxysmal hemoglobinuria as an antibody-complement complex. In their later work reactivating serum was added to the inactive hemoglobinuric serum and corpuscles and hemolysis resulted with the "cold-warm" experiment. These earlier experiments do not, however, deal with the point in question. There has arisen some divergence of opinion among later workers as to the capacity of the red blood cell to absorb antibody from inactive serum on exposure to the cold. Meyer and Emmerich<sup>5</sup> and Hoover and Stone<sup>6</sup> demonstrated that such absorption could take place, but Moss<sup>7</sup> could not confirm their results, and concluded that "union between auto-amboceptor and corpuscle takes place only at a low temperature, in the presence of complement."

This question can best be approached by a quantitative study of the lytic action of the inactive serum before and after exposure to corpuscles in the cold. The experiments were done as follows:

*Experiment A.* "P. Ina. Ser." was titrated by mixing with 0.3 c.c. normal human serum (complement) and then 0.25 c.c. 10 per cent. "P. Blood" added—incubated at 0° C. one-half hour and then warmed and incubated at 37° C. one-half hour.

*Experiment B.* Six complete lytic amounts (0.2 c.c. equals a complete lytic dose) of "P. Ina. Ser." were iced for one-half hour, with the sediment of four times six units (0.25 c.c. equals one unit) of 10 per cent. "P. Blood"—centrifuged in the cold and the serum removed for titration, as in A, by mixing with 0.3 c.c. normal human serum and then adding 0.25 c.c. 10 per cent. "P. Blood." Incubated at 0° C. for one-half hour, warmed, incubated at 37° C. one-half hour. The results are shown in Table II.

TABLE II.—Absorption of Antibody from Inactive Serum.

In each tube 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		
	A.—P. ina. Ser.	B.—P. ina. Ser. after 0° C. ½ hr. with Sed. P. Blood
	Hemolysis after 0° C. ½ hr.—warmed—37° C. ½ hr.	
0.4000 cc	Complete	Partial
0.2000 cc	Complete	Slight
0.1000 cc	Nearly complete	0
0.0500 cc	Very strong	0
0.0250 cc	Slight	
0.0125 cc	0	

Control: 0.4 cc P. ina. Ser. + 0.25 cc 10% P. Blood + 0° C. ½ hr. + warm + 37° C. ½ hr. = hemolysis, 0

In A the inactive serum was reactivated and gave complete hemolysis, with 0.2 c.c., the same minimum complete lytic dose as

<sup>5</sup> Loc. cit.

<sup>7</sup> Johns Hopkins Hosp. Bull., 1911, xxii, 238.

<sup>6</sup> Arch. Int. Med., 1908, iii, 392.



active serum plus complement, as shown in Table I—B. In B, as described here, the serum was exposed to "red blood cells" in the cold when no complement was present, as shown by the absence of hemolysis in the control. The serum was removed while still cold, and on titration, after adding complement, we find only "partial" hemolysis with 0.4 c.c. It is evident, therefore, that antibody was removed, and from the result about 85 per cent was absorbed by the corpuscles, in the absence of complement, on exposure to cold.

3. DISSOCIATION OF CORPUSCLE-ANTIBODY COMBINATION. In order further to understand the behavior of the autolysin it is necessary to determine whether or not there is ever a dissociation of antibody from corpuscle on subsequent elevation of temperature after they have been united by exposure in the cold. Meyer and Emmerich state that such dissociation does occur, and they were able to remove antibody from the sensitized red blood cells by washing them with warm NaCl solution. To determine this the following tests were made:

*Experiment A.* Two and one-half complete lytic doses of the "P. Ina. Ser." were added to the sediment of ten times two and one-half units of 10 per cent. "P. Blood," iced for one-half hour, centrifuged immediately in the cold, and the serum decanted and used for titration, as shown in Table III—A.

*Experiment B.* Two and one-half complete lytic doses of "P. Ina. Ser." were added to the sediment of ten times two and one-half units of 10 per cent. "P. Blood," iced for one-half hour. It was then warmed and incubated at 37° C. for one-half hour, centrifuged, and the decanted serum titrated just as in A. The results are shown in Table III—B.

*Experiment C.* This gives the titration of the "Ina. Ser." for this day, and shows 0.4 c.cm. as the minimum complete lytic dose of this serum. See Table III—C.

TABLE III.

A.—Titration of P. ina. Ser. after 0° C. ½ hr. with red blood cell and decant at once.

		Lysis.
0.4 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.	Faint trace
0.2 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed	0
0.1 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.	0

B.—Titration of P. ina. Ser. after 0° C. ½ hr., then 37° C. ½ hr. with red blood cell then decant.

		Lysis.
0.40 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		Partial
0.20 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.	Slight
0.10 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed	Trace
0.05 cc decant Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.	Faint trace

C.—Titration of P. ina. Ser.

		Lysis.
0.400 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		Complete
0.200 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.	Very strong
0.100 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed	Strong
0.050 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.	Slight
0.025 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		0
Control: 0.4 cc P. ina. Ser. + 0.25 cc 10% P. Blood		0

In A the inactive serum was exposed to a large body of corpuscles in the cold, and the serum was removed while still cold. As we have already seen, antibody is removed from serum so treated. In this experiment, when the decanted serum is reactivated and put through the "cold-warm" test, only a faint trace of hemolysis results with 0.4 c.c., and we may, therefore, conclude that practically all the antibody has been absorbed by the corpuscles. In B the same amount of inactive serum was exposed to the same amount of corpuscles for the same length of time. It is fair to assume that the same amount of antibody was removed from the serum by the corpuscles. But this inactive serum was left with its corpuscles for one-half hour in the incubator before separating it. On decanting and titrating it just as in A we find that 0.4 c.c. gives "partial" hemolysis and 0.1 c.c. gives a "trace." We have, therefore, demonstrated that antibody is dissociated from corpuscle at body temperature, for in this experiment about 25 per cent. of that absorbed was liberated. The corpuscle-antibody combination evidently is not an absolutely stable one. The difficulty of absorbing all the antibody from the serum, no matter how great the excess of corpuscles, is shown in the experiment already given, as well as in some of those that follow. This fact would suggest that an equilibrium is established on the part of antibody between the corpuscles, whose absorptive power is greatly enhanced by the action of cold, and the serum. This has its analogy in chemistry in the behavior of two immiscible solvents toward a solute. This fact, however, does not permit of an interpretation of the behavior of antibody on a definite and purely chemical basis in contrast to a biological one. That antibody would be returned in its entirety to the serum on more prolonged incubation is conceivable, but its demonstration is not essential for the purposes of discussion here.

4. ABSORPTION OF COMPLEMENT FROM ACTIVE SERUM. Apparently biased by the well-known behavior of complement and antibody in ordinary immune sera, that is, the capacity of an antibody to unite with its antigen in the cold, while complement remains free, Donath and Landsteiner maintain the view that cold is necessary only for the union of antibody and corpuscle and that complement unites at the higher temperature, with resulting hemolysis. They have, however, no experiments bearing directly upon this point. Eason concurs with this idea, but likewise without proof. Hoover and Stone were unable to get any hemolysis unless there was an exposure of corpuscles and inactive serum to the cold after complement was added, and they first suggested that cold was necessary both for the union of complement and antibody, as well as antibody and corpuscle. Meyer and Emmerich contend that cold is not necessary for antibody complement combination. They merely state their results and give no detailed protocols of the work upon which their conclusions rest. Moss states that "the complement

does not enter into the combination, or at least not permanently, at this temperature," for he was able to demonstrate complementary action in the decanted serum after active serum was chilled with corpuscles. His work may be criticised on the ground that it was not quantitative.

Whether complement does or does not enter into combination on exposure to the cold can best be determined by a titration of complement in active serum before and after the serum is exposed to corpuscles in the cold. The experiments are given in Table IV. In

TABLE IV.

## A.—Titration of Complement.

Amount of complement	In each tube 0.25 cc 10% Sensitized Sheep Blood.					
	P. Ser.	P. Ex. Ser.	P. ina. Ser.	N. H. S.	N. Ex. Ser.	G. P. Ser.
	Hemolysis after warming and incubating at 37° C. ½ hr.					
0.500000	.....	..	0			
0.400000	.....	0	0			
0.100000	Complete	..	..	Complete	Complete	
0.050000	Complete	..	..	Very strong	Complete	
0.025000	Partial	..	..	Slight	Very strong	
0.012500	Trace	..	..	Trace	Slight	Complete
0.006250	.....	..	..	.....	.....	Complete
0.003125	.....	..	..	.....	.....	Nearly complete

## B.—Titration of P. Ex. Ser.

0.40 cc P. Ex. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		Very strong
0.20 cc P. Ex. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.	Strong
0.10 cc P. Ex. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed	Slight
0.05 cc P. Ex. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.	0
Control: 0.4 cc P. Ex. Ser. + 0.25 cc 10% P. Blood		0

Table IV—A the titrations of complement were made against 10 per cent. sensitized sheep's blood. These sheep corpuscles were sensitized by the addition of antibody in the form of inactive serum of rabbit that was immune to sheep red cells. In the first column we see that "P. Ser." that is, active serum before exposure to corpuscles in the cold, is able to act as complement, and 0.05 c.c. is enough to induce complete hemolysis. In the second column, "P. Ex. Ser." is used. This, as stated above, is serum derived from the original defibrinated blood after it was iced for one hour. 0.4 c.c. of this serum has no complementary action, and induces no hemolysis whatever. That it cannot be said that the treatment destroyed complement, a control was done with normal human serum under absolutely identical conditions, and here we see (columns 4 and 5) that the exposure to corpuscles in the cold did not decrease the complement, but actually increased it by 100 per cent. This rather interesting and curious result has been obtained with several normal sera. The titer of "G. P. Ser." is given to show the degree of sensitization of the corpuscles used. "P. Ina. Ser." was also titrated against this hemolytic system to demonstrate its complete inactivation.

It is also necessary to demonstrate that complement is absent from the "P. Ex. Ser." as far as "P. Blood" is concerned. See Table IV—B. The control shows no hemolytic action of the "P. Ex. Ser." on "P. Blood." If we add complement ("N. H. S.") hemolysis results. This shows that the "P. Ex. Ser." contains antibody, about 15 per cent. of the original amount, and lack of hemolysis in the control must be ascribed to lack of complement. Here we have conclusive proof by two methods of the disappearance of complement from active serum, that is, its absorption from active serum by exposure to corpuscles in the cold. It is shown also that this disappearance of complement takes place only from that serum ("P. Ser.") containing a specific antibody, and not from normal serum. The evidence that complement unites with antibody only under the influence of cold will be given under Section 5.

5. ACTION OF COMPLEMENT ON RED BLOOD CELLS SENSITIZED WITH INACTIVE HEMOLYTIC SERUM. The previous experiments show that all the complement and 85 per cent. of the antibody was removed from the "P. Ex. Ser.," and must have been taken up by the corpuscles in the cold. The proof of this last assumption will be considered later. If complement is absorbed at one and the same time with antibody, can it or can it not unite with antibody subsequent to the union of the latter with corpuscles. And if it can unite subsequently, does this union take place in the warm or only under the influence of cold? The fact that complement is absorbed in the cold, which is quite contrary to the usual behavior of complement in immune sera, would certainly suggest that it must do so to act at all. The following experiments were done to determine the action of complement on corpuscles previously sensitized by exposure in ice to inactive hemolytic serum.

*Experiment A.* Four times two doses of the "P. Ina. Ser." (1.6 c.c.) and four units of 10 per cent. "P. Blood" (1 c.c.) at 0° C. one-half hour, centrifuged in the cold, decant the serum, and wash the corpuscles once with ice cold 0.8 per cent NaCl solution and suspend in 1 c.c. (original volume) of cold salt solution. These corpuscles, kept cold, were then used to titrate the "P. Ina. Ser." after it had been complemented with "N. H. S." The results are shown in Table V. The results obtained in the titration of the "P. Ina. Ser." against unsensitized cells (Table II—A) are reproduced for comparison.

*Experiment B.* In this case a larger proportion of "P. Ina. Ser." was added and left in the cold for a longer period of time with corpuscles to sensitize them, if possible, more strongly. They were then used as in Experiment A: Five times four doses of "P. Ina. Ser." and five units of 10 per cent. "P. Blood" were put at 0° C. for one hour, centrifuged in the cold, washed once with ice-cold salt solution, and the corpuscles suspended in the original volume (1.25 c.c.) of ice-cold salt solution. The titration with these strongly sensitized cells is shown in Table V—B.

TABLE V.

A.—Titration of P. ina. Ser. using Mod. Sensitized 10% P. Blood.

		Lysis	Tab. II-A
0.40 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood		Strong	Complete
0.20 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	0°C. ½ hr.	Strong	Complete
0.10 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	Warmed	Partial	Complete
0.05 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	37°C. ½ hr.	Slight	Strong

B.—Titration of P. ina. Ser. using Strongly Sens. 10% P. Blood.

		Lysis.
0.40 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	0°C. ½ hr.	Trace
0.20 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	Warmed	Trace
0.10 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood	37°C. ½ hr.	Trace
0.05 cc P.ina.Ser.+0.3 cc N.H.S.+0.25 cc 10% Sens.P.Blood		Trace

In this experiment we have a demonstration of a very curious inhibiting action. That this is not due to any substance originally present in the inactive serum is evidenced by the fact that in Experiment II—A this same serum in combination with complement gave active hemolysis. The result must be due in some way to the condition of the red blood cells as a result of their previous treatment, and there are three possible hypotheses upon which it may be explained: (1) That complement must unite with antibody at the same time that antibody unites with corpuscle; (2) deflection of complement; (3) complementoid inhibition.

To determine which of these explanations suffices, the following experiments were done:

*Experiment A.* This gives the titration of the "P. Ina. Ser." for this day.

*Experiment B.* Five times four doses of "P. Ina. Ser." (0.2 c.c. equals one dose) plus five units of 10 per cent. "P. Blood," iced for one hour, centrifuged, serum decanted, and the corpuscles washed once with ice-cold salt solution and suspended in the original volume (1.25 c.c.) of ice-cold salt solution. The corpuscle suspensions were divided into five tubes, 0.25 c.c. to each tube, the first four kept ice-cold and treated as shown in Table VI—B. The fifth tube was carefully warmed over a free flame; complement was then added and the tube kept at 37° C. for one hour.

TABLE VI.

A.—Titration of P. ina. Ser.

		Lysis.
0.40 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood		Complete
0.20 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	0° C. ½ hr.	Complete
0.10 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	Warmed	Nearly comp.
0.05 cc P. ina. Ser. + 0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. ½ hr.	Very strong
0.04 cc P. ina. Ser. . . . . + 0.25 cc 10% P. Blood		0
0.3 cc N. H. S. + 0.25 cc 10% P. Blood	37° C. 1 hr.	0

B.—Titration of P. ina. Ser. using Sensitized P. Blood.

		Lysis.
0.4 cc P. ina. Ser. + 0.3 cc N.H.S. + 0.25 cc 10% Sens. P. Blood	0° C. ½ hr.	Very strong
0.2 cc P. ina. Ser. + 0.3 cc N.H.S. + 0.25 cc 10% Sens. P. Blood	Warmed	Very strong
0.1 cc P. ina. Ser. + 0.3 cc N.H.S. + 0.25 cc 10% Sens. P. Blood	37° C. ½ hr.	Very strong
0.3 cc N.H.S. + 0.25 cc 10% Sens. P. Blood		Very Strong
0.3 cc N.H.S. + 0.25 cc 10% Sens. P. Blood	37° C. 1 hr.	0

In this case, as in the former, there is definite inhibition of hemolysis, as shown by comparison of A with B, for with the sensitized corpuscles twice the complete lytic dose only gives "very strong" lysis. These corpuscles, as did those in V—B, all give the same amount of lysis irrespective of the amount of inactive serum added, and this is the case even in the fourth tube, where complement alone was added. Our first hypothesis then must be discarded, for we have demonstrated by this fourth tube that complement can attach itself to antibody after antibody has been attached to corpuscle; but B—5 shows further that this union can take place only under the influence of cold, as already stated by Hoover and Stone, for if, after icing, tubes are carefully and quickly warmed over a free flame and complement added, as done here, the results are uniformly negative. This cannot be attributed to separation of antibody, for it has already been shown that this is rather reluctantly given off from the corpuscle on warming. Secondly, there is no ground for an explanation on the basis of "deflection of complement," so-called, for the less antibody added the less deflection possible, and the amount of hemolysis would be in inverse proportion to the amount of antibody added. This is not the case. The third hypothesis—complementoid inhibition—is an extremely interesting one. At the present day serologists, generally speaking, agree with Ehrlich's original conception that complement is composed of two fractions: the "endstück," or toxic part, which in hemolysis produces the lytic action, and a "mittelstück," by which the toxic portion is joined to the antibody. The "endstück" is thermolabile, and, therefore, absent in inactive serum, while the "mittelstück" is thermostable, and present in inactive serum. It has already been shown in this paper that the complement in serum of paroxysmal hemoglobinuria unites with antibody on exposure to corpuscle in the cold. There is, therefore, every reason to believe that complementoid will attach itself to antibody, and corpuscles when exposed to inactive serum take up antibody and antibody takes up complementoid in so far as this happens to be present, and will, therefore, block complement. That some hemolysis took place in the experiments can be attributed to the fact that all the antibody was not completely saturated with complementoid, for in none of the experiments on the serum of this case was there enough complement to completely activate all the antibody present. The question of complementoid in this serum has been studied further by a series of experiments, the protocols and discussion of which are reserved for a later paper; suffice it to say here that the presence of complementoid is shown.

6. MODE OF ACTION OF THE AUTOHEMOLYSIN. To review briefly then we have seen that antibody is taken up from inactive serum in the cold, that is, is absorbed in the absence of complement; that this combination is not absolutely stable, for a certain amount is

dissociated on elevation of temperature; we have also seen that complement is absorbed from active serum, together with antibody, in the cold, that complement unites with antibody only under the influence of cold, and finally, that the red blood cells exposed to inactive serum in the cold are more or less resistant to hemolysis on account of the complementoid present in inactive serum, the degree of resistance depending on the amount of complementoid present. These facts warrant the following statement as to the mode of action of the hemolysin: Antibody unites with corpuscle and complement unites with antibody only under the influence of cold, the lytic action being manifested on subsequent elevation of temperature. They cannot unite in any other way.

In order further to sustain this theory, we must be able to interpret the result of various experiments by it.

*Experiment 1.* One complete lytic dose (0.2 c.c.) of "P. Ina. Ser." plus 0.25 c.c. 10 per cent. "P. Blood," iced for one-half hour. Centrifuged in the cold and save "decant" serum for the next experiment. The corpuscles were suspended in 0.45 c.c. of cold 0.8 per cent. NaCl solution and 0.3 c.c. "N. H. S." added and incubated at 0° C. for one-half hour, warmed, then incubated at 37° C. for one-half hour. Result, hemolysis slight.

*Experiment 2.* The "decant" serum was added to the sediment of 0.25 c.c. 10 per cent. "P. Blood," with 0.3 c.c. "N. H. S.," iced for one-half hour, incubated at 37° C. for one-half hour. Result, hemolysis trace.

In the first experiment one complete lytic dose does not give complete hemolysis; there is evident inhibition, and this can now be explained on the basis of "Komplementoid Verstopfung." In the second experiment there was very little antibody present in the "decant" serum, but in the presence of complement, icing with untreated corpuscles gave slight hemolysis.

If corpuscles do take up antibody and complement in the cold, it should be possible to demonstrate this action also. For this purpose I have repeated one of Moss' experiments, using the exact proportion given by him and practically the same technique:

*Experiment.* 1 c.c. "P. Ser." (active) and 0.1 c.c. "P. Corp.," containing as little salt solution as possible, were iced for one-half hour, centrifuged in the cold, and corpuscles washed twice with salt solution at 0° C. They were suspended in 0.75 c.c. salt solution and incubated at 37° C. for one-half hour. Result, hemolysis slight. Complement added (0.25 c.c., "N. H. S.") and temperature maintained at 37° C. for two hours. No increase of hemolysis. Incubated at 0° C. one-half hour, then 37° C. for two hours. No apparent increase of hemolysis.

The result obtained here is different than that given by Moss, who found hemolysis after the addition of complement and without exposure to the cold. In my experiment hemolysis showed after

incubating the washed cells, and must have been due to anchored antibody and complement. This is the first positive result of this sort recorded, and it has been possible to duplicate it, although not constantly. The demonstrated dissociability of antibody and complement may be the explanation, although I am inclined to attribute it to the dissociation of complement, either "end-piece" or "mid-piece" from the combination, for it is readily conceivable that prolonged washing of corpuscles even with ice-cold salt solution might liberate end-piece or mid-piece of complement from corpuscle antibody combination. Experiments to determine this point have not been done. Hemolysis in this experiment was slight only, but if we analyze this it is found that we have but two and one-half complete lytic doses of serum (0.4 c.c. "P. Ser." was the minimum complete lytic dose on this day) added to the sediment of eight units of corpuscles. Naturally they are not highly sensitized and no greater hemolytic effect could be expected.

Meyer and Emmerich<sup>8</sup> give an experiment in which a tourniquet was placed about the finger of a hemoglobinuric, and it was immersed in ice water ten minutes. The blood then taken from the finger was centrifuged and the serum decanted. They do not state whether the corpuscles were washed or not. To the corpuscles was added normal human or guinea-pig serum, and without any further cooling, but merely on incubation, hemolysis resulted. They give this as an example of the union of complement to antibody in the warm, but there is no ground for their conclusion, for the result can be explained on the supposition that complement, as well as antibody, was already bound to the corpuscle "*in vivo*," and the complement added took no part in the reaction. The same result might have been obtained merely on the addition of salt solution without any complement. They do not state, however, that any such control was done.

It has not been possible to explain all of the varying results of experiments found in the literature on any one basis. It is a well-known fact that in cases where the paroxysms have been frequent the "cold-warm" experiment *in vitro* is very apt to be negative. In such cases we may presume a deficiency or absence of complement, and Meyer and Emmerich have shown that such did occur in some of their cases. Even in normal serum it has been frequently shown that there is considerable variation in the complement content from day to day. That absence of antibody occurs seems less likely on account of the difficulty of absorbing all of it even from defibrinated blood, but a deficiency might occur temporarily, although we know nothing as to the rapidity of its formation. That anti-complementary substances can and do occur is well known and Kumagai and Inoue appear to have demonstrated their presence in paroxysmal hemoglobinuria in a number of their cases.

<sup>8</sup> Loc. cit.



Such a formation could well account for the apparently spontaneous cures that take place from time to time in the course of this disease. Such a remission is shown in the history of this case. No such substance was present, however, during the period of observation. The negative and anomalous results so frequently obtained in test tube experiments with inactive serum are, however, explainable on the ground of complementoid inhibition. To reactivate inactive serum, complement should be added to it and mixed before corpuscles are added. By this technique positive results can be obtained which might otherwise be negative.

7. ETIOLOGY OF PAROXYSMAL HEMOGLOBINURIA. In spite of the work that has been done on paroxysmal hemoglobinuria the basic etiologic factor is still a matter of speculation. Considering the fact that we are apparently dealing with a true autolysin, our general knowledge of the production of such bodies certainly suggests that it may be the result of the rapid and extensive disintegration of homologous or autogenous red blood corpuscles within the body. In the first place, then, concealed and internal hemorrhage would seem to offer the proper predisposing factor. This aspect of the subject was reviewed by Eason in his second paper. Traumatic hemoglobinurias are on record, but while such hemorrhages are common, a resulting hemoglobinuria is extremely rare, is merely temporary and unlike the disease under discussion, in that cold is not a factor in the production of the hemoglobinuria.

Then, again, malaria is a condition that fulfils all the theoretical requirements for the production of a lysin. The conception of hemoglobinuric fever as a malarial manifestation is very earnestly disputed at the present time; in fact, the trend of opinion among authorities on tropical medicine is rather strongly in favor of its independent origin, but even were we to consider hemoglobinuric fever as a malarial manifestation, it would still be impossible to regard malaria as in any way etiologically related to paroxysmal hemoglobinuria, for on clinical grounds they are absolute antitheses as far as the mortality and the relation of climate to attacks is concerned. Moreover, a malarial history is very infrequently elicited in paroxysmal hemoglobinuria, and in spite of very careful experimental search, Barratt and Yorke<sup>9</sup> were not able to demonstrate an autolysin in the serum of cases of malaria or hemoglobinuric fever.

Finally, animal experimentation has been resorted to in an attempt to demonstrate the production of autohemolytic antibodies under ideal conditions. Ehrlich and Morgenroth<sup>10</sup> first studied this subject. They were unable to induce the formation of an autolysin in goats, experimentally, by the intraperitoneal injection of the laked blood of other goats, although an active isolysin developed.

<sup>9</sup> Ann. Trop. Med. and Hyg., 1909, iii, 152, Series T. M.

<sup>10</sup> Berl. klin. Woch., 1900, No. 21, p. 1 and 11.

They did not try the effect of cold on uniting any hypothetical auto-antibody to the red blood corpuscles. They argue that as the injection of an isolysin causes the production of anti-isolysin, so would the production of an autolysin lead to the formation of its antibody, but no such body could be demonstrated. That such an antibody need not develop, however, is abundantly proved by the fact that none has been demonstrated in the serum of hemoglobi-nurics in spite of the presence of the autolysin. Fejes and Kentzler<sup>11</sup> did succeed in one case of four when they injected rabbits, first with aleuronat solution intraperitoneally, and on the next day injected intraperitoneally 7 c.c. of autogenous blood plus the complete lytic dose of goose serum for this amount of blood. They state that the serum from one rabbit showed a hemolysin that behaved in all respects like that of paroxysmal hemoglobinuria in test tube experiments, but hemoglobin never appeared in the urine when the animal was chilled.

One fact that is particularly prominent is the association of syphilis, either congenital or acquired. Clinical observation of itself is quite impressive. Stempel (1902), quoted by Eason, found 30 per cent. positive in 77 cases in the literature. Of Kumagai and Inoue's 20 cases, 85 per cent. are given as luetic.

With the introduction of the Wassermann reaction these percentages have been still further increased. Of 37 cases now in the literature, including my own, on which the Wassermann reaction is reported, 33 or 90 per cent. are positive. It is, however, essential to bear in mind that this reaction is not specific; that is, is not dependent upon syphilitic antibodies for the complement absorption. This is evidenced by its occurrence in the serum of a large percentage of normal rabbits and in human serum just before and after death, irrespective of cause, by its high percentage in fram-besia, leprosy, relapsing fever, and malaria, and particularly by the fact recently reported by Noguchi, but still unpublished, that complement binding rarely took place when he used as antigen his pure culture of *treponema pallidum*, although the Wassermann reaction, done simultaneously, was positive.

It was in view of these facts that the luetin test was done in the case here reported. Noguchi<sup>12</sup> found his reaction positive in 96 per cent. of 23 hereditary cases and absent in all of 146 controls. As stated above, the reaction was positive in this case. It is, however, too new to warrant our placing absolute dependence upon it at this time.

That syphilitic infection does seem to bear definite relation is further shown by the investigation of Donath and Landsteiner. They examined the serum of 65 cases of general paresis *in vitro* for

<sup>11</sup> Zeit. f. klin. Med., lxxi, Heft 3 to 6, p. 194.

<sup>12</sup> Jour. Exp. Med., 1911, xiv, No. 6.

an autolysin, and found it present in 6 cases, two of which gave very marked reaction and 4 but slight. Using the 2 severe cases, the Ehrlich experiment, by icing a finger, showed hemolysis, but they were not able to induce an attack of hemoglobinuria in either. In 195 other cases of infectious and systemic disease, newgrowths and intoxications, including 28 cases of "lues," they were not able to show the presence of any hemolysin in the serum by their test tube experiments. They were led to suggest that the presence of the hemolysin in the serum is not sufficient of itself to induce the urinary manifestations of the disease and that vasomotor disturbances might be important contributing factors favoring the necessary temperature depression in the exposed tissues. Kumagai and Inoue have also recently reported such examinations for an auto-hemolysin. Thirty cases that were non-syphilitic by history and Wassermann reaction showed no lysin present. Their 13 cases of secondary syphilis also showed no lysin. Of 35 cases of tertiary and metasymphilitic disease 7 showed the presence of a hemolyzing substance. The Ehrlich experiment was performed on 4 of these, and 1 case gave a typical manifestation of paroxysmal hemoglobinuria. The other 3 responded by an attack which these authors consider a mild form of the disease; that is, albuminuria and urobilinogenuria with typical temperature and leukocyte changes but no hemoglobinuria.

We have, however, at our command one further and perhaps crucial test by which to determine the syphilitic or non-syphilitic nature of this disease, and that is the therapeutic test. Of the older writers, cited by Eason, Murri (1885) reports 2 cases and Kopp (1885) 1 case cured by inunctions of mercury. One of Moss' cases received "salvarsan," and while the Wassermann reaction was still positive at the end of four months, the attacks seemed to be beneficially influenced, although the autolysin was still present in the serum. Strange to say, of all the recent cases in literature not one has been followed to its definite and logical conclusion in this regard; that is, no observations have been made on any case in which, as a result of treatment with mercury and iodide and salvarsan, the Wassermann reaction has become negative. My own case still has a strongly positive reaction four weeks after the third injection of "salvarsan." I hope to be able to report observations later after the Wassermann has become negative.

**SUMMARY.** The observations here reported are based upon experiments with the blood of a typical case of paroxysmal hemoglobinuria.

The serum contains a complex hemolysin capable of dissolving the red blood corpuscles of the individual himself or other individuals by means of the cold-warm experiment. Positive results were obtained in all of the twelve examinations made at different times.

Auto-antibody is absorbed from serum in the absence of com-

plement, and on elevation of temperature is more or less completely but slowly dissociated.

Complement is absorbed from active serum on exposure to corpuscle in the cold. It will join with antibody after the latter has united with corpuscle, but this union takes place solely under the influence of cold.

Corpuscles sensitized with inactive serum show but slight hemolysis on the addition of complement as a result of complementoid inhibition.

As a result of clinical observation, the Wassermann reaction, the luetin test, and the serological studies in metasyphilitic disease, it seems safe to say that syphilis is the most important, possibly the only, etiologic factor in paroxysmal hemoglobinuria, but there are as yet no observations on the presence or absence of the hemolysin after the disappearance of the Wassermann reaction as a result of syphilitic treatment.

## A CASE OF DELAYED DEVELOPMENT IN A BOY TREATED WITH THYMUS GLAND.<sup>1</sup>

By C. G. KERLEY, M.D.,

PROFESSOR OF PEDIATRICS IN THE NEW YORK POLYCLINIC AND HOSPITAL,

AND

S. P. BEEBE, M.D.,

PROFESSOR OF EXPERIMENTAL THERAPEUTICS, CORNELL UNIVERSITY MEDICAL COLLEGE,  
NEW YORK.

THE physiology of the thymus gland is very imperfectly understood. No one of the ductless glands appears to have a more active part in the economy, especially in the younger years of life, and yet its complete removal is not accompanied by those striking manifestations which follow removal of the thyroid or adrenal. It cannot be concluded, however, that because the removal of a gland is not followed by an acute death, it plays no important part in nutrition. The evidence afforded by removal of the sexual glands is proof on this point.

The laboratory investigations are not altogether in accord. Certain points, however, seem to be fairly well established. The thymus remains in an active condition during the presexual life of an animal, but with the onset of sexual maturity it undergoes a retrogression which finally amounts to an almost complete atrophy. The involution of the thymus appears to be a more rapid process when the sexual glands become mature. When castration is performed before puberty the thymus does not show the same degree

<sup>1</sup> Read before the American Pediatric Society, Hot Springs, Va., May 30, 1912.

of involution found in normal animals. Some observations point to the belief that thymectomy in guinea-pigs is followed by an earlier ripening of the sexual glands, while other experiments with chickens show that thymectomized birds have much smaller sexual glands than the controls. There appears to be an intimate relation between thymus and sex glands in respect to their mutual development and also with respect to the effect on nutrition.

The second point in which there seems to be some agreement in the experiments is in the relation of thymus removal to the development of the skeleton. While thymectomy is not followed by an acute death, the animals subjected to the operation do not in many cases grow to the same size, have the strength, or show the resistance to infection exhibited by controls. In respect to the bones, they are of a smaller size, are softer, and the epiphyseal line is broader and more irregular compared with controls.

These conclusions seem to have a fairly definite relation to the results obtained in the treatment of the case about to be described.

There has been no active substance found in the thymus which compares with adrenalin or iodothylin. For therapeutic purposes the whole gland, either fresh or dried, has been administered in most instances. Until thymus implantation is perfected or until the active principle is discovered, such a method seems the only one available.

In February, 1910, a mother referred by Dr. Brooks Wells brought her son, aged sixteen years and four months, to consult one of us (Kerley) regarding what she termed "a failure of development." She stated that the boy had made no perceptible growth in over two years, that his genitals were small and undeveloped, and that the testicles were not in the scrotum. She was greatly worried, fearing that the boy would never be a man. Her statement further was to the effect that the boy was mentally sound, was active in play, and normal in mentality, as proved by his standing in school. He was in classes corresponding to other boys of his age.

Examination showed the boy to be delicate in appearance, normal in all respects excepting that he was undersized, his height being 56 inches and his weight 76 pounds stripped, both weight and height being about that of a boy, aged eleven to twelve years.

The penis was small and shrunken, the testicles were very small, and although there was no retention and they could readily be brought into the scrotum, they rested in the canal a greater part of the time. There had never been an erection of the penis, and there was neither pubic hair nor hair in the axilla.

The treatment instituted was that of lightening the school work, more hours in bed, and a suitable diet. Tincture nucis vomici, arsenic, and cod-liver oil comprised the medication. The patient was seen at about one month intervals during the following nine months. At this time there was a gain of 3 pounds in weight.

His height was the same and there was no change whatsoever in the sexual development. The family were extremely troubled and requested that every effort be used in the boy's interest. At the suggestion of Dr. Beebe, all medication was discontinued and desiccated thymus extract, 15 grains daily, was prescribed.

During the first six months of thymus administration the genitals, penis, and testicles perceptibly enlarged, and after nine months' use the first erection occurred when aged seventeen years and ten months. This was new and novel and amused the patient very much. At the completion of one year of treatment, when aged eighteen years, hair appeared on the pubis and in the axilla. He had gained 1 inch during the year, standing 57 inches, and had gained 11 pounds, weighing 87 pounds.

During the next six months, which brings us to April of this year, 1912, when aged eighteen years and six months, he had gained 2 inches in height, bringing him at the present time to 59 inches in height, and gained  $8\frac{1}{4}$  pounds in weight, increasing the weight to  $95\frac{1}{4}$  pounds. The testicles have remained in the scrotum during the last six months. The voice changed in February of this year, when he was aged eighteen years and four months.

In the eighteen months under treatment there was a gain of 3 inches in height after he was aged seventeen years, and  $19\frac{1}{4}$  pounds in weight when there had been no growth according to the mother's statement for two years and nine months before.

The sexual organs are apparently normal and well developed. The use of the thymus might be considered a coincident in a case of retarded development; such cases of late development, however, are most unusual. No claims are made for the thymus. We appreciate that one case proves but little.

Six other cases of slow growth or retarded development are under observation with thymus at the present time. These cases will be reported later and will help to establish the point that naturally will arise in the mind of the reader whether or no thymus was operative in the case reported or whether it is to be looked upon as a coincident, and that the phenomena we observed would have taken place without its use.

---

### ACUTE PANCREATITIS.<sup>1</sup>

BY JOSEPH M. KING, M.D.,

PHYSICIAN TO THE SISTERS' HOSPITAL, LOS ANGELES, CALIFORNIA.

THE following case is so suggestive, and presents so much that is typical of acute pancreatitis, that its history is given first:

<sup>1</sup> Read in abstract before the Southern California Medical Society, December 6, 1911.

CASE I.—F. J. C., male, aged thirty-six years, married, a native of Minnesota, by occupation a foreman in a stone cutting establishment, 5 feet 8 inches tall, weighing 210 pounds, was taken sick August 8, 1910. His family history was negative. He himself had had measles, mumps, chickenpox, and, when aged nine years, "bilious remitting fever," with which he was sick three months, and from which he fully recovered. He had never suffered from any venereal diseases, nor did he use tobacco. Once in ten days or two weeks he consumed large quantities of beer while playing cards, but did not become intoxicated. He was always a hearty eater. He had never suffered from any symptoms of stomach or gall-bladder disease. August 7 he had slight chest pains and a little discomfort in the epigastric region, which he attributed to "taking cold." He went to work as usual on August 8, feeling better, but at 10 A.M. was taken with an agonizing, cutting, tearing pain in the epigastric region. Upon being given a drink of whisky his pain was increased, and was also felt in the back, being most marked in the lower dorsal and upper lumbar region to the right of the spine. This excruciating pain, in spite of many doses of morphine hypodermically, continued for about a week. It was accompanied by continual vomiting of greenish material. He had but few symptoms of collapse, although the pulse became rapid. He had moderate fever after the first day. For three days he had obstinate constipation which did not yield to any form of treatment. High enemas were expelled without fecal matter, but he passed a little flatus. On the fourth day the administration of a half ounce of castor oil caused his bowels to move several times.

After a week he still had much pain in the back, but none in the abdomen. Laparotomy had been positively declined. The patient came under personal observation August 19. He was found resting easily, without febrile temperature, the pulse 90, full and regular. He did not have pain, neither was he vomiting. He was slightly jaundiced. The heart and lungs were negative. The abdomen was somewhat rigid. The liver edge, sharp and regular, was felt about two and one-half inches below the costal margin. It was not enlarged upward, nor was it tender. The spleen could not be palpated. In the median line, just below the margin of the liver, and insensibly shading into it, midway between the xiphoid and umbilicus an indefinite mass was felt, which was rather tender. No continuation of this mass could be traced either to the right or left. There was no special muscle rigidity or tenderness over McBurney's point. The bowels were somewhat constipated, and the stools were "putty colored." The urine was rather scanty, and contained bile, but did not contain albumin or sugar. There were no casts. Examination of blood showed: Hemoglobin (Dare), 80 per cent.; erythrocytes, 4,500,000; leukocytes, 12,000, of which a differential count gave polymorphonuclears, 70 per cent; lymphocytes, 22 per

cent; large mononuclears and transitionals 6 per cent; eosinophiles, 2 per cent.

He gradually improved and insisted on going about, visiting my office two or three times, the first occasion being on September 8. At this time the liver was still enlarged, but the mass in the median line was not palpable, and the jaundice had disappeared. He did not feel well, however, had a little tenderness in his abdomen, a temperature of 99° F., and did not regain his appetite or strength.

On September 15 he had a second attack, with fever, vomiting, rapid pulse, slight jaundice, clay colored stools, etc., but without pain. He developed a slight cyanosis, which persisted throughout the remainder of his illness. The mass was again palpable, being more easily felt than in the earlier part of his illness. He showed some improvement by September 20, losing his temperature and rapid pulse. Laparotomy was urged, but firmly declined, as was all operative interference throughout his illness, although frequently advised. On September 26 his temperature, which had been subnormal for two or three days, again rose, with the physical signs of pleurisy in the left chest.

From this time until his death on October 27 his fever was remittent, usually ranging from 98° to 99° F. in the morning to a maximum of 102° to 104° F. in the afternoon. Sweats were frequent. His pulse was continuously above 100, averaging about 115. It was regular. The respirations varied from 22 to 30, and were often irregular, and accompanied by dyspnea. The urine was scant, never containing any albumin, but always showed an increased amount of indican, and also contained bile. Sugar was not present until about a week before his death, and then only a trace, and was not constant. The jaundice, although slight, was persistent. Emesis was a constant symptom, and one of the most pronounced throughout his sickness. He usually did not vomit his food, particularly solid food. The vomitus was fluid, olive green or greenish brown in color, of a very offensive odor, and the amount often so large that it seemed to exceed the patient's fluid intake, as high as twenty-eight ounces being expelled at one time.

During the last two weeks of his illness, the vomitus was often dark brown and fetid, proving on chemical examination to contain altered blood.

More or less tympanites were constantly present; belching and the passage of flatus from the bowels were also frequent. The bowels were never more than slightly constipated. The feces were sometimes dark brown and well formed, occasionally liquid, and occasionally the typical stool of obstructive jaundice. They were not fatty.

On October 21 the patient had a violent chill, with a sudden rise in temperature to 104.4° F. and a pulse rate of 160, followed by collapse, with rectal temperature of 96, 2° F. From this he rallied



and two days later his stool was exceptionally offensive, with much pus, and full of a material closely resembling sand in consistency and color. From this time on the stool contained a varying amount of a liquid or semiliquid slate-gray substance, with metallic luster and offensive odor, often containing shreds of tissue. On October 27 the patient had four hemorrhages from the bowels in the course of a few hours, three of them profuse and bright red in color, but not clotted when passed. After this he rapidly sank, and in a few hours died.

An autopsy was performed by Dr. Stanley P. Black fifteen hours after death. There was much fat necrosis in the omentum, mesentery, and the peripancreatic fat. The liver was enlarged and fatty. The gall-bladder was filled with altered bile, which was, however, readily emptied into the bowel. One small calculus was found in the neck of the gall-bladder, but the ducts were patulous. The spleen was enlarged to twice its normal size, and contained a wedge-shaped anemic infarct. The foramen of Winslow was closed and the lesser omental sac was converted into an abscess cavity, in which lay the pancreas, so broken down that scarcely a vestige of normal pancreatic tissue remained. A perforation about 0.5 cm. in diameter was present in the transverse colon; this communicated with the lesser omental cavity, and fresh clots were adherent to its edges. The heart showed slight fatty infiltration. A plastic pleurisy was present on both sides, but more marked on the left. Otherwise the organs were normal.

Acute pancreatitis occurs usually in adults, aged from twenty to fifty years. It is about twice as frequent in males as in females. It is more often seen in fat, strong individuals than in the thin or feeble, and possibly a little oftener in those addicted to the use of liquor. A careful reading of the reported cases leads one to the conclusion that many of the patients had one or more previous attacks of acute pancreatitis from which they recovered, the symptoms being wrongly ascribed to the gall-bladder or stomach and duodenum. This is not to be wondered at in view of the fact that about half of the cases of pancreatitis are accompanied by gallstones. Only when a more severe attack occurred for which an operation was performed, or in which death resulted, with an autopsy, was the true diagnosis of pancreatitis made.

Opie<sup>2</sup> has pointed out and emphasized the close relationship between acute pancreatitis and cholelithiasis, and has laid great stress upon the effects of stone in the common duct obstructing or occluding the ampulla of Vater, thus converting the bile duct and the duct of Wirsung into a common tube, and so permitting the gall-bladder to force bile into the duct of Wirsung. It has been proved experimentally by Flexner<sup>3</sup> and others that bile will produce

<sup>2</sup> Diseases of the Pancreas, 1910, second edition.

<sup>3</sup> Jour. Exper. Med., 1906, viii, 167 to 177.

necrosis of the pancreas. It had also been proved experimentally that the injection of even small quantities of duodenal contents into the pancreatic duct will cause necrosis of the pancreas. Invasion from this source might be expected to be most common; but the results of bacteriological examination in cases of pancreatitis have not been uniform, and the mucous membrane of the ampulla of Vater is so arranged that, in the dead body at least, it has not been found possible to force material from the duodenum past it. Moreover, the necrotic parenchyma may contain no organisms, the products of inflammation being found only at its margins, and then only after the lapse of an appreciable interval of time after the onset of the trouble.

Williams and Busch,<sup>4</sup> however, have performed experiments on animals which make it seem probable that some cases of acute pancreatitis may be caused by the regurgitation of duodenal contents into the diverticulum of Vater, the previous passage of gallstones having dilated the opening in the papilla, and thus rendered the diverticulum more patent than in health. Furthermore, in about one individual in ten the duct of Santorini is the larger, and affords an outlet for the secretion of the greater part of the pancreas. The opening of the duct of Santorini is not as well guarded as is the diverticulum of Vater, and when this anomaly of the duct exists the entrance of duodenal contents through it may explain some cases of acute pancreatitis. Infections by direct extension through the wall of the intestine and also through the medium of the blood stream or lymphatic channels have also been suggested as possible causes of pancreatic inflammation, but no clinical data have been brought forward to support these hypotheses.

Injuries in the upper abdomen, although occasionally causing pancreatic hemorrhage, give rise to an inconsiderable portion of the cases under discussion. Mumps gives rise to a certain number of cases of acute pancreatitis by metastasis; about 10 per cent. in Egdahl's<sup>5</sup> collective investigation. Such cases are usually mild, eventuating in recovery. On the whole it cannot be said that we have as yet accurate knowledge of the etiology of the condition.

The initial symptom, occasionally after a day or two of gastric uneasiness, is usually agonizing, almost unbearable pain felt in the upper abdominal or lower thoracic region, exceptionally in the lower abdomen or about the appendix, and occasionally referred to the back, in the lower dorsal region. It may be paroxysmal or continuous, but its distinguishing characteristic is its great severity. It has been explained on the ground that it was caused by the stretching of the parietal peritoneum. This pain is soon accompanied by nausea and vomiting of a greenish watery fluid. Belching

<sup>4</sup> Trans. Assoc. Amer. Phys., xxii, 304 to 314.

<sup>5</sup> Johns Hopkins Hosp. Bull., 1907, No. 193, 130 to 135.

is also usually present, and is often persistent throughout the attack. Obstinate hiccough occasionally occurs.

At the onset the temperature is normal or subnormal and the pulse is slow and full, but the pulse becomes rapid early in the attack. Symptoms of collapse soon appear, with rapid, weak, thready pulse and subnormal temperature. While collapse usually occurs early it may be delayed for a day or two, or be absent altogether. This condition of shock is apt to be prolonged. If the patient survives, these symptoms are usually succeeded by fever of a moderate degree, although occasionally the disease pursues its entire course without any elevation of temperature. The pulse remains rapid in a majority of cases, and the pain with nausea and vomiting continues. Cyanosis, particularly of the face, is often a well-marked symptom. In about 25 per cent. of the cases a slight jaundice appears. In about 50 per cent. an obstinate constipation is present, in which the bowels cannot be moved by any agent. Usually a little flatus is passed, particularly if high enemas are given. In three to five days the bowels move spontaneously or under the influence of some mild cathartic, such as castor oil. The abdomen is somewhat tympanitic, rather tender all over, and especially so in the epigastrium, a little to the right of the median line. One may sometimes feel an indefinite mass halfway between the xiphoid and umbilicus. It is rarely possible to palpate the acutely inflamed pancreas, and a mass is felt only after a collection of fluid occurs in the lesser omental cavity, therefore this sign is of little value for early diagnosis.

The mind usually remains clear throughout the disease. Blood-good,<sup>6</sup> however, in speaking of the second stage of pancreatitis, says: "In addition to fever and leukocytosis there is usually a delirium which we seldom see in other abdominal abscesses. In the 3 cases which I have observed the delirium has impressed me as a characteristic sign. The delirium may be described as that observed in typhoid infection."

Death, which may occur in the first few hours, most frequently occurs between the second and fourth day. If the patient survives, in about a week the violent symptoms abate, and while the belching, nausea, and vomiting are apt to be persistent, diarrhea or only moderate constipation succeed to what appeared at first like intestinal obstruction; the temperature is lower; the pulse fuller; the jaundice may disappear; the pain is gone; and only epigastric tenderness remains. Occasionally, as in the case here reported, and in one reported by Dick,<sup>7</sup> the patient may seem convalescent, and a free interval supervenes before the stage of pancreatic abscess. Or, indeed, he may recover, as occurs in possibly one-fourth of the cases.

<sup>6</sup> *Internat. Clinics*, 14th series, i, 264.

<sup>7</sup> *Edinburgh Med. Jour.*, 1910, v, 3, 217 to 234.

In a majority the symptoms only diminish somewhat in intensity, and after ten days or two weeks the fever often becomes irregular in type, sometimes accompanied by chills, the vomiting and belching still persist, sweating occurs, especially at night, the mass is more readily felt, and occasionally the whole site of the pancreas may be outlined by palpation. Percussion over the mass gives flat tympany, due to the interposition of the stomach. Infective conditions, as pleurisy or pericarditis, may now appear, and hemorrhage from the stomach or bowel may be added to the picture.

The urine presents no special characteristics. Febrile albuminuria and a few hyaline or granular casts are usually present. Sugar is rarely found, as glycosuria does not occur so long as only a small portion of the gland functionates, which is usually the case. Indican is sometimes present. Lipase, a fat-splitting ferment, is occasionally found in the urine, which is strong presumptive evidence that the pancreatic fat-splitting ferment is present in the peritoneal cavity, from which source it is being extracted by the urine.

The reaction of Cammidge,<sup>8</sup> about which so much has lately been written, does not seem to be so successful in the hands of others as in those of the author. Cammidge says: "My experience with the improved method has been most satisfactory, for in every case where pancreatitis has been found to be present, the urine has given more or less marked reaction, corresponding to the extent of the lesions. Normal urines have given no reaction, and control cases . . . where there was no pancreatic lesion, have also proved negative."

In careful studies recently reported by Wilson,<sup>9</sup> Kinney,<sup>10</sup> Whipple,<sup>11</sup> and others little value is accorded to the test. Wilson, reporting on 504 tests from Mayo's clinic, says: "The end results, judged by Mr. Cammidge's own criteria, must be considered as a means of diagnosing disease of the pancreas, as both valueless and misleading. There is no apparent clinical relationship between disease of the pancreas and any of our various types of end reaction."

Kinney, reporting from Dr. Deaver's service in the German Hospital, Philadelphia, says: "Very little dependence can be put upon a negative reaction, and a positive reaction can only be considered of value as a confirmatory examination."

The blood usually shows an early but comparatively slight increase in leukocytes, without any great relative increase of the polymorphonuclear variety; this is to be expected, the condition being toxic rather than infective. Later, after gangrene and infection have taken place, a typical polymorphonuclear leuko-

<sup>8</sup> Surg., Gyn., and Obstet., 1906, iii, 3, 440 to 444.

<sup>9</sup> Ibid., 1910, xi, 2, 156 to 159.

<sup>10</sup> AMER. JOUR. MED. SCI., 1910, No. 6, cxi, 878 to 883.

<sup>11</sup> Johns Hopkins Hosp. Bull., 1910, No. 236, xxi, 339 to 352.

cytosis may appear. In protracted cases anemia of the secondary type is common.

The stools are but rarely fatty; they may or may not present the appearance of obstructive jaundice, depending upon the amount of obstruction of the common duct, due either to gallstones or pressure of the enlarged head of the pancreas. In perforation of the bowel hemorrhage may occur, and pus is found in the stools. In a few instances a necrotic slough of the pancreas has been passed from the bowels, as first observed by Chiari,<sup>12</sup> in 1862, the patient being well seventeen years later.

Not all cases follow this regular type, especially in the mode of onset they may vary from the rule. Some have little pain, only a sense of epigastric uneasiness; in others, fever is entirely absent for quite a time; occasionally, nausea is not pronounced; and collapse may not occur. Some, indeed, present at the onset only the symptoms of one of the continued fevers. The following case illustrates pancreatitis of gradual onset:

CASE II.—Mr. J. H. H., married, aged fifty-five years, a native of Michigan, travelling salesman by occupation, became ill early in August, 1905. He had a slight afternoon temperature and some nausea, but no vomiting. His abdomen was a little tender, and he had slight constipation. After about a week with these symptoms he took to his bed. When first seen on August 14 he was found with a temperature of 102° F., a slow, full, dicrotic pulse of 70, without nausea, somewhat constipated, with a little tympanites, and abdominal tenderness. The urine contained a trace of albumin and a few granular and hyaline casts, but was otherwise normal. A provisional diagnosis of typhoid fever was made, but after a day or two this had to be abandoned, for while the pulse and temperature curve were like those of typhoid, the spleen was not palpable, no rose spots appeared, the Widal test was negative, and above all the leukocyte count was 16,000, with the polymorphonuclears predominating. About August 21 the patient began to have nausea again, and had occasional vomiting of a greenish fluid. He also had for the first time a sensation of weight in the epigastrium, which directed particular attention to that region. The abdomen was not now rigid nor distended, and after a couple of days, although the patient was stout, with a fat abdomen, a sense of epigastric resistance was noticed. This developed so that by the fourteenth day of illness an indefinite mass, corresponding exactly to the location of the pancreas, could be mapped out. Pain became more pronounced, and vomiting more frequent, changing from green to blackish brown. The pulse also increased in rate and became feebler, sweats occurred, and the temperature assumed more of the septic type. A diagnosis of acute

<sup>12</sup> *Wien. med. Woch.*, 1876, p. 292; 1880, xxx, 139.

pancreatitis was made, and operation was advised. The abdomen was opened through a median incision by Dr. George W. Lasher, on September 4, who found fat necrosis and a necrotic pancreas, which was drained. The patient did not rally, and died September 6.

Autopsy by Dr. Stanley P. Black about fourteen hours after death revealed a pancreas every part of which was necrotic. Fat necrosis was present in the abdominal fat, and the gall-bladder was filled with altered bile and "sand." The intestines showed no evidence of typhoid fever.

Cases of this kind, as pointed out by Bloodgood, seem to pass through the stages of hemorrhage and necrosis symptomless, the patient not feeling ill until secondary bacterial infection occurs.

The morbid anatomy varies with the duration of the disease. In some cases death occurs suddenly, and nothing is found except hemorrhage into and about the gland, with little evidence of inflammation. Such cases have been designated pancreatic apoplexy, or pancreatic hemorrhage.

In others dying within the first few days the gland is usually found enlarged and firm, and with necrotic areas dark red or reddish black in color. The whole organ is seldom involved, and sharply defined areas of normal tissue are present. All of the structures of the pancreas, the parenchyma, interstitial tissue, and blood-vessels are alike implicated in the necrosis.

Hemorrhage into the organ is so constant a feature as to have given the disease at this stage the name of acute hemorrhagic pancreatitis.

Much discussion has arisen as to whether the necrosis precedes or follows the hemorrhage, but the most widely accepted view seems to be that the necrosis of the vessels sets free the blood.

The hemorrhage varies much in its amount and extent, sometimes being scarcely noticeable, and at other times the whole lesser omental bursa is distended, and blood oozes through the foramen of Winslow. The peripancreatic tissues are also often infiltrated with blood, and a blood-stained fluid is practically always present in the peritoneal cavity.

The products of acute inflammation are not constant or widespread, and are found usually only at the margins of the necrotic masses. Indeed, it is generally believed that bacteria if present have no etiological relationship to the lesion, but are secondary invaders.

Gradually the pancreas into which hemorrhage has taken place becomes necrotic, shading off from a chocolate color to a slate-gray, forming a foul-smelling mass, in which the pancreas may be wholly spaccellated, and to which the term acute gangrenous pancreatitis has been given. With the invasion of bacteria suppuration takes place. Adhesions close the foramen of Winslow, and there is an accumulation of fluid in the lesser peritoneal cavity. This may

erode the retroperitoneal tissue, and the pus burrows down into the left lumbar region; or perforation through the diaphragm, or into the stomach, duodenum, or transverse colon may occur. Portions of the necrotic pancreas may be discharged by the bowel, as previously noted.

In some cases multiple abscesses or only one or two large abscesses are found, without any evidence of hemorrhage or gangrene; or suppuration may be diffuse throughout the gland; or abscess of the lesser peritoneal cavity may be present. Owing to their anatomical characteristics these cases are usually classed by themselves as acute suppurative pancreatitis. Clinically, however, no such distinction can be made, for while in many of them the onset is gradual, the symptoms are less severe, and they tend to run a chronic course; in others, as in the case reported by Cheney,<sup>13</sup> they have exactly the same symptomatology as the acute hemorrhagic form.

In all but the suppurative conditions Opie prefers the term "hemorrhagic necrosis of the pancreas" as more nearly describing the pathological changes.

Fat necrosis, a conspicuous feature of the disease, is always present to a greater or less extent. It was first described by Balser<sup>14</sup> in 1882, while Fitz,<sup>15</sup> in the greatest contribution ever made to this subject, first pointed out the relation between it and pancreatitis. It is usually limited to the fat of the abdominal cavity, the areas being most numerous and often coalescent in the region of the pancreas, with discrete foci in the omentum, mesentery, and perinephritic fat. Areas have also been observed in the subcutaneous fat, and in the subpleural and pericardial fat. These, however, are rare. The spots vary from one to several millimeters in diameter, often surrounded by a narrow zone of cell proliferation, and with their opaque tallow-like appearance, present a sharp contrast to the normal fat about them. When small and numerous they have been mistaken for tubercles.

Langerhans<sup>16</sup> showed that fat necrosis was caused by the splitting of fat into fatty acids and glycerin, the fatty acids being deposited within the cell and the glycerin absorbed. The fatty acids later combine with calcium salts.

This necrosis, as has been abundantly proved by numerous experiments, is caused by the setting free of the pancreatic secretion with its fat-splitting enzyme, directly into the tissues, and is, as Opie has said: "A consequence of pancreatic disease, and bears much the same relation to lesions of the pancreas as does jaundice to hepatic disease. Its presence gives evidence that the pancreatic secretion has been diverted from its normal channels into the interstitial tissue of the organ and into neighboring organs."

<sup>13</sup> Jour. Amer. Med. Assoc., 1909, lii, 1819 and 1820.

<sup>14</sup> Virchow's Archiv, 1882, xc, 520.

<sup>15</sup> Boston Med. and Surg. Jour., cxx, Nos. 8, 9, and 10.

<sup>16</sup> Virchow's Archiv, 1890, cxxii, 252.

While this condition is occasionally found with other pancreatic lesions, in them it is not abundantly distributed, and is only constant with hemorrhagic or gangrenous pancreatitis. It is, as Fitz pointed out, much less frequently associated with suppurative lesions.

In the event of recovery these areas of fat necrosis may entirely disappear by a process of absorption, with a proliferation of the fixed connective-tissue cells.

The diagnosis of acute pancreatitis is not easy, and is usually made with certainty only at operation or autopsy. Fitz,<sup>17</sup> who gave the first accurate description of the symptoms, said, in speaking of the diagnosis: "The symptoms are essentially those of a peritonitis beginning in the epigastrium and occurring suddenly, during ordinary health, without obvious cause. The diagnosis, therefore, is based on pain, tenderness, and tympany limited to the region of the pancreas, and on the gradual development of a deep-seated peritonitis in the same place. The differential diagnosis lies, practically, between an irritant poison, perforation of the digestive or biliary tract, and acute intestinal obstruction.

In perforations of the hollow viscera, the tenderness and rigidity are much more marked, but the pain is not so agonizing, nor are pain and collapse so prolonged as in acute pancreatitis.

In intestinal obstruction, also, the severe constitutional symptoms are not present early to any such degree, and abdominal palpation excites colicky pains, while in pancreatitis the absence of indican from the urine, the decreased intestinal peristalsis, the greater intensity of pain, and the passage of flatus from the bowel are valuable indications.

Acute pancreatitis has also been mistaken for fulminating appendicitis, but in that condition the pain is more apt to be about or below the umbilicus, with a considerable rise of temperature, and the signs of a beginning general peritonitis appear early.

Biliary colic may simulate acute pancreatitis, especially as many cases are preceded by typical biliary attacks; but in pancreatitis the greater severity and long continuance of pain, the wider diffusion of the pain, the collapse so frequently present, and the appearance later of an indefinite tumor mass in the epigastrium should put the physician on guard, and cause acute pancreatitis to be considered; moreover, in suppurative cholangitis, the pain often radiates to the right subscapular region, and tenderness and muscle spasm are greater in the right upper quadrant.

Ptomain poisoning may be suggested by the early symptoms, but it is to be remembered that this condition is usually attended by diarrhea from the beginning, which is a rare condition in the first days of an acute pancreatitis.

The prognosis is bad. Fully 60 per cent. of recognized cases die.

<sup>17</sup> Loc. cit.



Many succumb to the disease from the second to the sixth day, the third being the day of greatest fatality. It is now a well-established fact that trypsin poisoning is responsible for the death of those cases which do not go on to gangrene. The intensity of the poisoning depends on the amount of the gland destroyed by the necrosis; this explains the varying degrees of toxicity, from that which kills in a few hours to that seen in mild cases which eventuate in recovery.

The prolonged shock is also ascribed to this same toxic agent. Some investigators have attributed the early deaths, particularly those occurring within the first twenty-four hours, to a reflex from the sympathetic ganglia near the pancreas, analogous to death caused by a blow over the solar plexus.

Cases caused by or accompanied by gallstones seem to have a less favorable outcome than those in which they are not present. In Egdahl's<sup>18</sup> collective investigation of 105 cases, 30 cases out of 44 with gallstones died, while only 17 out of 32 cases not complicated by stone ended fatally.

Women seem to have a better prognosis than men. Less often attacked, they seem, when ill with this disease, to have more resistance, and a smaller percentage succumb during the hemorrhagic stage.

The suppurative forms are liable to become somewhat chronic and, with efficient drainage, may get well. Undoubtedly many cases recover which, owing to the difficulty of diagnosis, have been ascribed to other causes.

The treatment is surgical. Aside from symptomatic treatment, all that avails is free drainage. A few cases, possibly one-fourth, recover without surgical treatment.

In mild doubtful cases gastric lavage and rectal alimentation put the stomach and duodenum at rest, and so favor the reduction of inflammation and swelling of the ducts, and thus, by reestablishing drainage through the common duct, favor recovery.

The intense pain requires repeated injections of morphine, and the collapse may be combated by normal saline injections. Strychnine and diffusible stimulants are also of value. The intestinal distention, if excessive, may be relieved by high rectal injections. Cathartics are useless for the obstinate constipation of the first few days.

Much discussion has arisen as to whether these cases should be operated on early. Fitz, in his original article, disapproved of it, saying of laparotomy: "An operation which, in the early stages of this disease, is extremely hazardous."

Guleke,<sup>19</sup> however, has virtually proved that the cause of death is the trypsin intoxication, and this being the case, a laparotomy

<sup>18</sup> Loc. cit.

<sup>19</sup> Archiv f. klin. Chir., 1908, lxxxv, 615 to 662.

done as early as the condition of the patient warrants, permits the escape of a considerable quantity of peritoneal fluid which contains this ferment.

In a good many cases, as in Case II, reported by Dick,<sup>20</sup> recovery occurred after an early exploratory laparotomy, in which a few ounces of bloodstained fluid escaped and fat necrosis was observed; but the pancreas was not disturbed, and the abdomen was closed without drainage. How much good an operation of this extent may do is problematical. Drainage is always indicated, as it still further empties the peritoneal cavity, and tends to limit further necrosis of the pancreas. Some operators have made incisions into the gland, but the great tendency to hemorrhage from this organ and the difficulty of controlling it must not be forgotten. Ransohoff<sup>21</sup> has reported a case in which death evidently took place from hemorrhage, although the gland itself was not incised. The gall-bladder and ducts should be investigated and calculi removed, but the condition of the patient is usually such in these early operations that this procedure must be deferred to a later date. The extent of operation is still a moot question, and must depend largely on the patient's condition.

With the formation of pancreatic abscess the indication for extensive drainage is clear, and the earlier this is performed, before the patient is exhausted and septic, the better the prognosis. Even then a large percentage die. When it is remembered, however, that without drainage death is inevitable the duty of the physician is plain. In those cases in which an abscess can be made out in the region of the left kidney it may be reached through a lumbar incision, but in all other cases the abdominal route, with drainage through the gastrohepatic or possibly through the gastrocolic omentum would seem preferable, because of the greater accessibility and opportunity for more careful exploration.

---

## THE EFFECT OF COLD AIR UPON THE CIRCULATION IN HEALTHY AND SICK INDIVIDUALS.<sup>1</sup>

BY THEODORE B. BARRINGER, JR., M.D.,  
ASSOCIATE ATTENDING PHYSICIAN, NEW YORK HOSPITAL.

THE following observations were carried out at the House of Relief to determine whether in cold air we possess an agent of any therapeutic efficiency for combating the vasomotor and cardiac

<sup>20</sup> Loc. cit.

<sup>21</sup> Ann. Surg., 1910, xli, 5, 670 to 681.

<sup>1</sup> Read before the Section in Medicine of the New York Academy of Medicine, February 20, 1912.

weakness which so often complicate infectious diseases and post-operative conditions, and the treatment of which by drugs is so unsatisfactory.

Preliminary experiments were conducted on 9 adults, who were either convalescent from operations or suffering from indifferent medical conditions like constipation, but whose circulations were apparently normal. They were in bed at least twelve hours before any observations were made. Systolic pressures were then taken in a warm room, every ten or fifteen minutes for an hour or longer, until the individual readings differed but slightly. Then the bed containing the patient was rolled from the warm room to the roof ward, which is open on three sides to the air. Each patient was well covered with blankets and a skull-cap, so that only the face was exposed. Blood-pressure readings were then made by the auscultatory method every five or ten minutes, by the same person, using a Stanton sphygmomanometer.

The following table summarizes our results:

Name.	Age.	Average systolic blood pressure in warm room.	Maximum blood pressure out-of-doors.	Maximum blood pressure attained in	Duration increased blood pressure.	Length of exposure.	Temp. out-of-doors.
S.	34	108	115	15 minutes	30 minutes	4 hours	21° F.
F.	45	120	145	30 minutes	4 hours	4 hours	22
....	..	118	118	....	....	45 minutes	38
....	..	111	140	3 hours	6 hours	8 hours	14
W.	18	104	108	20 minutes	40 minutes	1 hour	22
....	..	98	108	5 minutes	5 hours	12 hours	18
S.	45	107	124	15 minutes	2 hours	8 hours	44
....	..	105	110	15 minutes	1 hour	8 hours	25
G.	16	100	108	10 minutes	25 minutes	1 hour	22
R.	19	114	114	....	....	8 hours	14
D.	46	122	132	3 minutes	30 minutes	1 hour	22
K.	17	108	118	2 hours	6 hours	8 hours	14
H.	31	120	124	8 minutes	30 minutes	1 hour	30

Average blood pressure before exposure, 110; average blood pressure after exposure. 120.

Eleven of the 13 experiments showed a rise of blood pressure varying between 4 and 35 millimeters of mercury, the average increase being equivalent to 10 millimeters. The maximum pressures were reached in from three minutes to three hours, persisted for varying lengths of time, and were often succeeded by a fall to the initial levels before the exposure had terminated. This is not a marked effect, for we found that 5 of these same men when kept quietly in bed in the ward showed an average daily variation of blood pressure amounting to 15 millimeters. Only the fact that in a majority of cases the rise occurred after a few minutes of exposure enabled us to attribute it to the cold air. It might be surmised that these initial rises were due to psychic or accidental causes rather than to the cold air. Had this been so the effect would have been transient, instead of persisting as it did. The pulse rate

showed approximately no change. The diastolic pressures also varied but slightly, in the several cases in which they were read.

Van Oordt<sup>2</sup> has carried out somewhat similar experiments, exposing his patients, however, entirely uncovered to a temperature averaging 44° F., for periods varying between five and thirty min-

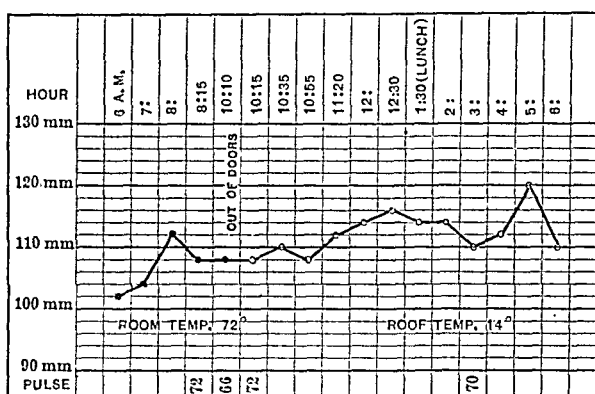


CHART 1.—Blood pressure reaction in normal individual with face exposed to cold air. Portions between circles represent observations made out-of-doors.

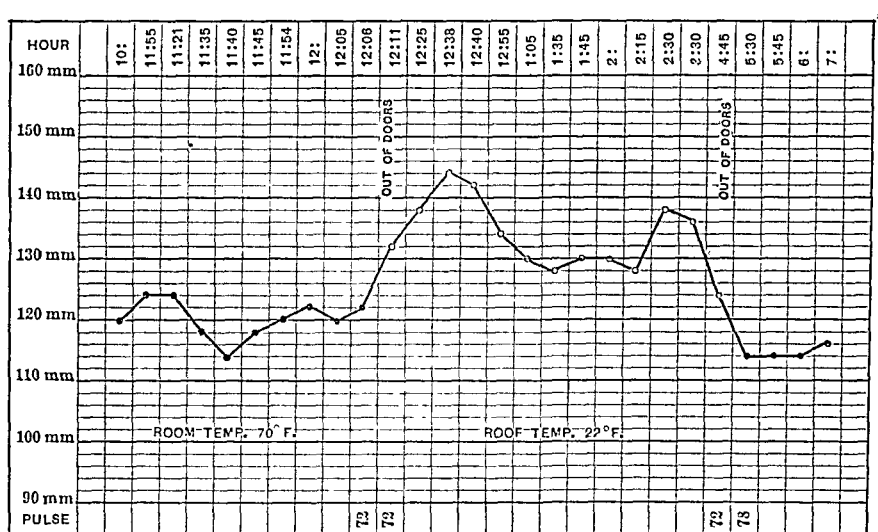


CHART 2.—This chart shows by far the most marked and consistent reaction we obtained. The patient was a Chinese, suffering from constipation. A temperature of 38° produced no reaction, one of 22° a marked reaction (represented above), and one of 14° F. a still more marked and persistent rise.

utes. In 5 normal adults he noted an average rise of systolic blood pressure equivalent to 12 millimeters of mercury. This is but slightly more than the rise in our men, who were, with the exception of the face, entirely covered; that is, stimulation of the nasal mucosa by air at a temperature varying between 14° and 23° F. caused about the same pressor effect in our subjects (presumably through

reflex action on the vasomotor centre) as was caused in Van Oordt's subjects, by exposure of the entire body to a temperature of 44° F.

Under the same conditions as obtained in the experiments on normal men, observations were then made in various forms of disease.

The following table summarizes our results with cases of lobar pneumonia. All of the men were actively sick, running high temperatures:

Name.	Age.	Day of disease.	Average syst. blood pressure in warm room.	Maximum syst. blood pressure out-of-doors.	Time exposed.	Temperature out-of-doors.
C.	31	3	125	126	8 hours	23° F.
O.	26	3	103	98	1 hour	23
O. C.	21	7	112	112	8 hours	23
E.	24	5	123	121	8 hours	35
S.	54	8	140	142	9 hours	18

The results were quite negative. There was no constant effect on the pulse.

We have observations on but 1 case of typhoid fever, in a man, aged twenty-seven years. The blood pressures were very low, varying between 60 and 100 almost from the first week.

	Ward.	Out-of-doors.	Ward.	Out-of-doors.
Day of disease . . . . .	32-38	38-44	44-46	46-48
Temperature . . . . .	99°-102°	99°-101.6°	99°-102°	normal 48th day
Average systolic blood pressure . . . . .	78	104	102	115
Average pulse rate . . . . .	85	95	104	80
Temperature of air . . . . .	68°	52°-50°	68°	42°-50°

It seems as if in this one case the out-of-doors treatment had a favorable effect on the blood pressure.

The following are the results in 2 cases of tuberculosis running high temperatures, 1 case of serofibrinous pleurisy, with moderate fever, and 1 case of cardiac insufficiency from chronic myocarditis.

Name.	Age.	Disease.	Average systolic blood pressure in warm room.	Maximum systolic blood pressure out-of-doors.	Maximum pressure attained in	Time of exposure.	Temp. out-of-doors.
Y.	31	Acute pneumonic phthisis	108 112	109 122	.... 7 hours	8 hours 8 hours	33° F. 13
M.	36	Tuberculous pleurisy	102 92	108 110	30 minutes 13 hours	7 hours 8 hours	33 10
C.	25	Sero. fib. pleurisy	98	105	8 hours	8 hours	34
M.	44	Chronic myocarditis	150	148	....	8 hours	25

The fourth experiment is the only unquestionably positive one. There was no constant effect on the pulse in these cases.

Our attempts to influence the pulse or blood pressure being thus without result in practically all except one of our sick cases, it seemed worth while, in view of Van Oordt's experience, to see whether a greater exposure of our patients would have any positive effects. Accordingly, comparisons were made between the patient's condition when out-of-doors and warmly covered and when out-of-doors and covered with only a sheet. The time of exposure varied between thirty and thirty-five minutes. Cases with moderately high fever were selected, and as soon as the patient complained of feeling chilly the experiment was stopped.

The following table shows our results:

Name.	Diagnosis.	Average blood pressure before exposure.	Temp. immediately before exposure.	Max. blood pressure during exposure.	Temp. after exposure.	Difference in pulse.	Temp. of air.
S. G. Y.	Pneumonia	108	103.0°	134	102.0°	None	38° F.
	Pneumonia	109	103.0	108	101.8	96-92	38
	Acute pneumonic phthisis	138	102.8	142	102.0	110-108	38
		110	103.2	110	102.0	104-102	20
		118	....	120			

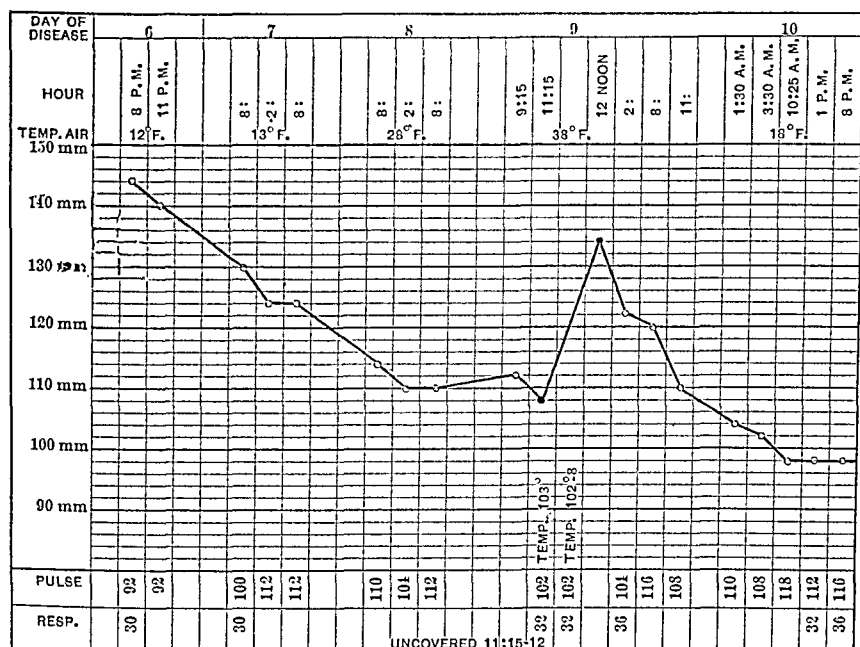


CHART 3.—Effect upon the blood pressure of a patient with pneumonia and delirium tremens when out-of-doors and covered and when only covered with a sheet.

The pulse was slowed and the temperature lowered in four experiments. The blood pressure was not markedly affected except in 1

case, a chart of which is given above. The patient was suffering from pneumonia and delirium tremens, but was quiet for some hours at the time of the experiment.

The summary of our results in the cold-air treatment of various infections shows that of 16 experiments carried out on 12 patients but 2 were positive, judging from the time of onset and degree of the rise in blood pressure. The heart was slowed in 4 of the experiments, in which the patient was covered with only a sheet. No sweeping conclusions can be drawn from an experience with so few cases, but the generally negative results make it seem improbable that the therapeutic value of cold air in diseases of adults is due to any dynamic effect on the circulation. That cold fresh air is of the utmost value in the treatment of infectious diseases is unquestionable, but its *modus operandi* must be sought in other directions.

CONCLUSIONS. 1. A slight rise of systolic blood pressure is produced in normal adults by exposure of the face to cold air. This rise persists for a varying length of time, and is often succeeded by a fall to the initial level, although the exposure be continued.

2. In 16 experiments carried out on 12 adults suffering from different infections the systolic blood pressure was increased decidedly but twice, as a result of exposing the patients to cold air.

## LEUKOCYTE AND DIFFERENTIAL COUNTS IN WARD AND OPEN AIR TREATMENT.

BY T. G. ORR, M.D.,

HOUSE PHYSICIAN, NEW YORK HOSPITAL (HOUSE OF RELIEF).

FEW observations have been made comparing the leukocyte counts of patients in the usual hospital ward with counts made in the open air. Cabot<sup>1</sup> states that prolonged cold bathing decreases the number of white cells in the peripheral circulation and dry cold does the same. Lenkei<sup>2</sup> found that cold-air baths caused a rise in leukocytes in a majority of cases, amounting to as much as 9.8 per cent. Van Oordt<sup>3</sup> has carried out some very complete experiments along this line. He exposed naked persons to an average temperature of 7° C., making leukocyte counts immediately before and at varying lengths of time after exposure. His conclusions were that cold air causes a leukocytosis in the skin capillaries which is produced by thermotaxis, and that this leukocytosis continues as long as the naked body is exposed to the cold air. Upon rewarming the

<sup>1</sup> Clinical Examination of the Blood, p. 189.

<sup>2</sup> Pester Med. Chir. Presse, May, 1910, xlv, No. 20.

<sup>3</sup> Zeit. f. Diätetische u. physikal. Therapie, 1905-6, ix, 338.

skin there is a gradual decrease in the leukocytes until the end of an hour, when the change ceases, leaving, however, an absolute increase in the number of leukocytes.

Our object was not to determine if there was any transient change in the leukocyte or differential counts when patients were moved into the open air, but to learn if there was any constant difference between the counts in the ward and those out-of-doors in the regular routine treatment of bed patients.

We have made total leukocyte and differential counts upon patients at times varying from one hour to three or four days after moving the patients from the ward into the open air, or from open air into ward. The time allowed to elapse between the counts depended upon the nature of the case. In cases that were apt to have marked changes in the number of white cells, the counts were made with only a few hours intervening, and those in which there was little change clinically, counts were made at longer intervals. In the open air only the face of the patient was exposed. All but 3 of our patients were kept constantly in bed during the experiments. To avoid digestion leukocytosis nearly all of the counts were made from three to five hours after a meal. Digestion leukocytosis, however, is hardly to be considered in the febrile cases, because of their comparatively low proteid diet. In the latter cases the counts were made at the height of the disease, and crises or sudden changes in the intensity of the infections were avoided.

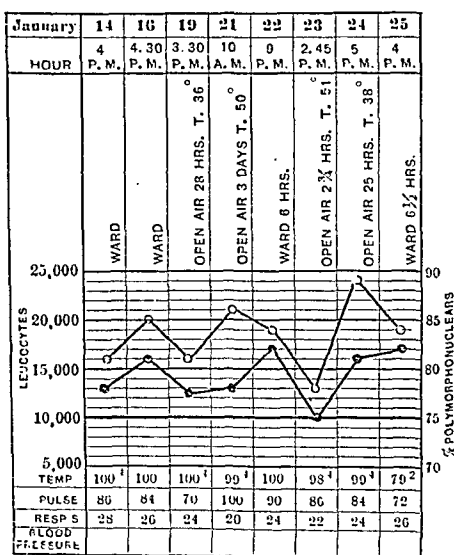


FIG. 1.—Leukocyte chart of febrile case.

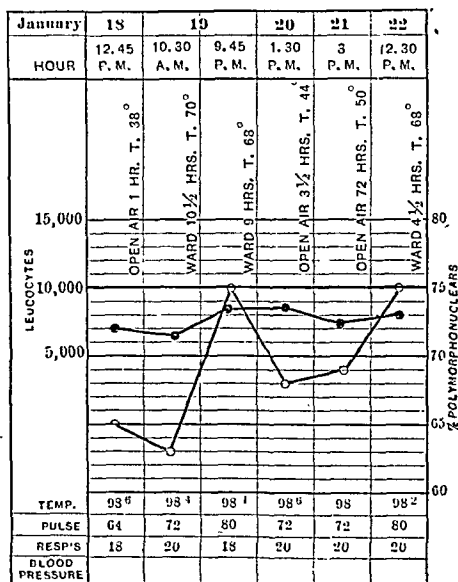


FIG. 2.—Leukocyte chart of afebrile case.

In making the differential counts, attention was given only to the percentage of polymorphonuclears, they being the cells of chief interest in a majority of acute infections.



The method of charting the counts is shown in the accompanying leukocyte chart (Figs. 1 and 2). This chart was suggested to us by the charts used by Gibson<sup>4</sup> and Hewitt<sup>5</sup> in their papers on the leukocyte and differential counts in acute surgical diseases. Ten thousand leukocytes and 75 per cent. polymorphonuclears are considered the upper limits of normal, and are placed on the same normal line in the chart.

Observations were made upon 10 afebrile and 8 febrile patients. The accompanying table shows the results obtained.

Disease.	Ward.					Open air.				
	Average temperature of ward.	Average temperature of patient.	Number of counts.	Average total leukocytes.	Average percent. of polymorphonuclears.	Average temperature of air.	Number of counts.	Average total leukocytes.	Average percentage of polymorphonuclears.	Percentage of increase or decrease of total leukocytes.
<b>AFEBRILE PATIENTS.</b>										
Tenotomy (postoperative) . . . . .	68°	98.2	3	8,500	49.3	25°	3	9,166	48.6	+ 7.8
Entamebic dysentery (convalescent) . . . . .	68°	98.4	3	8,166	71.3	32°	2	6,750	75.0	-17.3
Syphilis of liver . . . . .	68°	98.5	3	9,377	82.2	36°	3	9,333	84.3	- 0.4
Chronic cardiac valvular disease . . . . .	68°	98.6	2	6,750	54.5	34°	3	7,166	58.6	+ 6.1
Pharyngitis (convalescent) . . . . .	68°	98.6	2	9,000	63.0	47°	2	9,250	61.5	+ 2.7
Constipation . . . . .	68°	98.6	3	7,500	71.0	41°	3	7,666	67.3	+ 2.2
Hernia (postoperative) . . . . .	68°	98.2	2	8,750	60.0	40°	2	9,000	57.5	+ 2.8
Hernia (postoperative) . . . . .	68°	98.4	1	7,000	71.0	30°	1	6,000	72.0	-14.2
Hernia (postoperative) . . . . .	68°	99.0	3	12,166	68.6	32°	2	11,666	68.6	- 4.1
Malaria (convalescent) . . . . .	68°	98.6	2	9,000	50.5	52°	2	8,000	47.0	-11.1
<b>FEBRILE PATIENTS.</b>										
Lobar pneumonia . . . . .	68°	104.1	3	11,333	93.6	37°	3	11,833	94.6	+ 4.4
Lobar pneumonia . . . . .	68°	102.3	2	10,500	89.5	28°	4	10,375	89.5	- 1.2
Lobar pneumonia . . . . .	68°	103.1	3	27,500	90.0	39°	3	27,166	89.6	- 1.2
Lobar pneumonia . . . . .	68°	103.5	2	16,250	89.5	24°	3	14,833	90.6	- 8.7
Serofibrinous pleurisy . . . . .	68°	100.5	3	8,333	77.3	33°	2	7,500	74.5	- 9.9
Chronic pulmonary tuberculosis . . . . .	68°	102.2	5	8,600	78.2	27°	5	8,200	75.0	- 4.6
Chronic bronchitis . . . . .	68°	100.0	4	15,377	83.5	35°	4	12,777	83.5	-16.8
Acute bronchitis . . . . .	68°	101.5	3	19,166	84.0	19°	3	19,833	87.0	+ 3.4

Of the afebrile patients, there were 5 who showed an increase and 5 a decrease in total leukocytes, 4 an increase, 1 no change, and 5 a decrease in the polymorphonuclear counts. The total leukocytes of 2 of the 8 patients with fever were increased and 6 decreased in the open air. The polymorphonuclear percentages were increased in 3 cases, they were unchanged in 2 and decreased in 3 cases.

**CONCLUSIONS.** 1. There is no constant change in the total leukocyte or polymorphonuclear counts in afebrile patients when

<sup>4</sup> Annals of Surgery, April 1906, xliv, 485.

<sup>5</sup> Ibid., December 1911, liv, 721.

treated in the open air with only the face exposed as compared with counts in the ward.

2. In the majority of patients with fever and leukocytosis there is a small percentage decrease in the total leukocytes when treated in the open air with only the face exposed as compared with the count when treated in the ward. Under like conditions there is no constant change in the polymorphonuclear counts.

These experiments were carried out at the House of Relief in the service of Dr. T. B. Barringer, to whom I am much indebted for advice and assistance in the preparation of this paper.

---

### FATAL PNEUMOTHORAX FOLLOWING EXPLORATORY PUNCTURE.<sup>1</sup>

BY HUGHES DAYTON, M.D.,

ASSOCIATE ATTENDING PHYSICIAN, NEW YORK HOSPITAL.

In a paper on Accidents and Deaths from Exploratory Puncture of the Pleura,<sup>2</sup> the statement was made that the importance of pneumothorax after exploratory puncture depended upon the condition of the patient at the time of its occurrence and upon the physical state of the perforated lung, which might permit contraction of the puncture or favor extreme or progressive pneumothorax. This was based entirely upon a study of cases in the literature as no instances of this accident were found in the records of the New York Hospital during the twelve and a half years under consideration. Since then 2 fatal cases of this character have forced the conclusion that the physical state of the opposite lung may be of even greater importance.

Case No. 175,676, a widow, aged fifty-eight years, was admitted to New York Hospital on February 7, 1912, complaining of pain in the chest and cough. The only significant portion of her previous history was that of chronic cough for many years. In February, 1911, she was treated in the New York Hospital for an attack which was diagnosticated as pneumonia and resembled it in history, blood findings, and course, though the sputum was never blood-tinged. Cough continued until the present illness. About December 29, 1911, she had cough, chills, and fever every night, moderate sputum, never blood-tinged, and pain in both chests increased by coughing. Since January 4 she had been confined to bed and had lost considerable weight. On February 7, examination showed emaciation. Over both lungs there were slightly woody resonance, high-pitched

<sup>1</sup> Read before the New York Academy of Medicine, Section on Medicine, May 21, 1912

<sup>2</sup> Surg., Gyn., and Obstet., 1911, xiii, 607.

voice, and occasional sibilant and subcrepitant rales. Posteriorly, over the left base, where signs of consolidation had been present a year before, were impaired resonance and diminished breathing. The sputum was scanty, thick, mucopurulent. Six specimens were negative for tubercle bacilli. The temperature usually ranged between 98° F. and 101° F. or less each day, with respirations at first 36 to 46, later 22 to 26, and pulse 92 to 104. The urine was that of chronic interstitial nephritis. The leukocytes numbered about 10,000, of which about 70 per cent. were polymorphonuclears. On February 22 the left chest posteriorly from the seventh rib to the base and extending out four inches from the median line showed dulness and many subcrepitant rales; over the upper part of this area were bronchial breathing, voice, and whisper.

Two days later I noted in the seventh and eighth spaces, about two to two and a half inches from the median line, a small area over which cavernous breathing and whisper were heard only after productive cough. After unproductive cough there were heard coarse, almost musical moist rales. Within a few minutes after coughing the signs suggestive of a cavity would disappear completely excepting occasional rales. Below the above area were dulness, diminished breath and voice sounds to the base of the lung. The patient's general condition improved and she was allowed to sit up. *On the morning of March 5, she did not feel well and had some dyspnea.* At 8 A.M. the temperature was 102°; respiration, 24; pulse, 100. Physical signs were unchanged. Aspiration of the right chest was ordered. Hearing of this, I reached the ward just as a needle had been inserted, at 4.45 P.M., in the sixth right intercostal space just internal to the vertebral border of the scapula. The needle was carefully inserted about one inch and nothing obtained. The patient complained, immediately after its withdrawal, of intense pain at the site of puncture and in the front of the right chest, then showed severe and increasing dyspnea and cyanosis. Signs of subcutaneous emphysema appeared over an area three or four inches in diameter around the site of puncture. Over the entire right chest were dull tympany and very distant breath sounds. The right border of cardiac dulness was displaced from the right to the left sternal margin. A diffuse apex-beat was indistinctly felt in the fifth space 13 cm. out. At 4.55 P.M., systolic blood pressure was 90, pulse 108, feeble and irregular in frequency. Magendie's solution, caffeine sodiosalicylate, and adrenalin were administered, but the patient became more cyanotic and was unconscious by 5 P.M., when blood pressure was only 60, pulse 120. The note over the right chest gradually became more dull and lost its tympanitic quality. Through a needle inserted in the third right interspace in the midclavicular line air was expressed during expiration, apparently not under good pressure. Death occurred at about 5.10.

Autopsy by Dr. R. G. Stillman showed the diaphragm extending to the fifth interspace on the right side and to the fourth on the left. The right lung seemed collapsed in part and the heart was displaced to the left. The right pleural cavity was dry and was filled over the apex of the upper lobe of the lung with dense fibrous adhesions. The puncture wound in the sixth right intercostal space, 5 cm. from the median line, occupied a position where the pleura was free from adhesions and corresponding to the apex of the lower lobe. The right upper lobe was somewhat lacerated by its removal but otherwise appeared normal. The surface of the lower lobe was smooth, glistening, and grayish-pink. No evidence of a puncture of the lung was found. A few encapsulated fibrous nodules were scattered through this entire lung. Two or three of these were calcareous. The left pleural cavity was entirely obliterated by firm adhesions. The left lung on section presented a dark-red surface from which on pressure a moderate amount of red, frothy fluid exuded. Along the posterior border of the lower lobe was an area of indurated tissue, about 4 by 9 cm., in which could be seen a multilocular cavity occupying almost all of this portion of the lung. The lining of this cavity was smooth. Opening into it were two or more dilated bronchioles. The bronchial mucous membrane was deeply injected and covered with mucopus. The walls of the bronchi appeared to contain an excessive amount of cartilage which in many places exhibited calcareous infiltration. Besides these signs of adhesive pleurisy at the right apex and right pneumothorax, with chronic pleurisy and chronic fibroid phthisis with cavity formation in the left lung, other lesions included those of chronic interstitial nephritis, chronic interstitial splenitis, perihepatitis, fibrous goitre, and a calcified uterine fibroma.

Of the possible causes of pneumothorax, entrance of air through the needle can be positively excluded, as the needle was attached, before introduction, to a Connell vacuum bottle with active suction. That air could not have entered subsequently through the puncture wound in the chest-wall was shown by the presence of a drop of blood over the wound until it was closed with collodion. That it was not the result of laceration of the adherent right apex was shown by the absence of signs of antemortem hemorrhage in any of the lacerations produced during removal of the lung at autopsy. Although no puncture hole could be found in the lung, the occurrence of a small perforation by the needle seems proved by exclusion. Operation upon the chest would have been ineffective because the asphyxia was due to the collapse of the only serviceable lung.

The chief object in reporting this case is to emphasize the statement made in my previous paper<sup>3</sup> that the greatest danger exists in puncturing cases in which chronic inflammatory processes are

<sup>3</sup> Loc cit.

present. That assertion was made with reference to the danger of causing hemorrhage or pleural reflexes when puncturing the diseased lung. As regards the production of pneumothorax, some claim that it is most likely to occur when pleural adhesions are present or consolidation of the lung prevents closure of the puncture. Others think it occurs most often when the pleura is normal and the lung diseased, especially when there is softening in the lung near the pleural surface but not involving it. In the case which I have reported and one to which I shall refer briefly, the punctured lung tissue was absolutely or practically normal.

When the patient's general condition is not too poor, when the perforated lung is in such physical condition as to permit closure of the puncture and so prevent extreme and progressive pneumothorax; and when the opposite lung is in good condition, unilateral pneumothorax may pass almost unobserved. In a patient (2S 58, 486) who died in the New York Hospital in 1897 of acute pancreatitis after his right chest had been repeatedly explored, the autopsy showed pneumothorax of the right pleural cavity. The right lung was collapsed and inflation under water showed two small punctures, but the lungs were otherwise normal. In this case there were no subjective symptoms of pneumothorax.

A second case of fatal pneumothorax following exploratory puncture was a longshoreman, aged thirty-nine years, who was admitted to the Medical Division (No. 181442) on February 29, 1912, apparently suffering from lobar pneumonia involving the right lower lobe. Fever continued and signs of consolidation of the right lower lobe and the apex of the upper lobe persisted, especially near the spine of the scapula, where they suggested an interlobar empyema. Two punctures near the apex of the right lower lobe yielded no fluid. Signs of a suppurative process in the left shoulder developed and the patient was transferred to the Surgical Division. An abscess was drained by an incision through the deltoid muscle. The pus contained streptococci. A septic temperature continued; the x-rays showed infiltration of much of the right lung, and signs of consolidation of the apex of the right upper lobe became more marked. A large subcutaneous abscess appeared behind and below the left shoulder and this was incised. At about 2.30 P.M. on April 12, a needle was inserted in the upper portion of the left chest posteriorly in search of other collections of pus. A few minutes after this puncture the patient complained of a choking sensation and became dyspneic with profuse sweating. Physical signs of pneumothorax developed in the left chest and death from asphyxia occurred at 12.10 A.M. on April 13.

Autopsy by Dr. Schultz showed universal, thick, pleural adhesions over the right lung which was filled with innumerable tubercles. The apex of the left lung contained many tubercles and the overlying pleura was adherent. The rest of the lung was collapsed. The

site of the puncture was not found, but was probably in or near the adherent pleura. There was osteomyelitis of the scapula and head of the humerus involving the shoulder joint. As in the first case, it was the almost complete disability of the unwounded lung which led to the fatal termination from pneumothorax.

The point which I would emphasize above all is that the most serious and sudden results of the occurrences of pneumothorax due to exploratory puncture follow injury, not of the diseased, but of the efficient lung, when, as in two of the cases reported, the diseased lung is so incapacitated by consolidation and adhesions as to be incapable of adjusting itself to the unusual task. In the presence of a chronic inflammatory pulmonary process we are thus confronted with a choice of evils. Puncture of the area of chronic consolidation may result in hemorrhage or serious accident from pleural reflexes; puncture of the opposite normal lung may cause fatal pneumothorax. It is true that puncture of a normal lung rarely causes pneumothorax, but when it does do so, under such circumstances as existed in the cases reported, it is equivalent to signing a death-warrant. With these facts before us the conclusion seems inevitable that in the presence of probable chronic inflammatory disease of the lung, exploratory puncture should be restricted to cases in which there are good reasons for suspecting the existence of purulent exudate which would require surgical treatment.

---

## TUBERCULIN THERAPY IN SURGICAL TUBERCULOSIS.

BY THOMAS WOOD HASTINGS, M.D.,

PROFESSOR OF CLINICAL PATHOLOGY IN THE CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.

### PART I. ARTICLES AND MONOGRAPHS.

KOCH'S ERA. The use of specific therapy in tuberculosis began with the era established through the discovery of Koch's tuberculin. Koch<sup>1</sup> recommended the injection of old tuberculin after careful experimental work upon healthy and tuberculous guinea-pigs.

Among the first to experiment upon the same line were two investigators in this country, Trudeau<sup>2</sup> and de Schweinitz,<sup>3</sup> both of whom obtained results corroborating Koch's experimental work, and it is safe to say that since their time no more important and convincing experiments have been done along the same line. In reviewing the literature dealing with experimental active immunization for tuberculosis, one is impressed with the fact that experimental evidence in favor of injection of tuberculin is far from

convincing; on the other hand, when one studies the literature of tuberculin therapy relating to the treatment of patients afflicted with chronic and resisting forms of tuberculosis, one is impressed with the fact that tuberculin is an extremely useful adjunct to the better known methods of therapy. We have had little experience with pulmonary tuberculosis, and for a consideration of this subject the numerous papers by Koch,<sup>1</sup> Petruschky,<sup>4</sup> Goetsch,<sup>5</sup> Mueller,<sup>6</sup> Turban,<sup>7</sup> Weicker,<sup>8</sup> Spengler,<sup>9</sup> Baudach,<sup>10</sup> Trudeau,<sup>11</sup> Denys,<sup>12</sup> and Sahli<sup>13</sup> should be consulted. More recent papers by younger observers, Hammer,<sup>14</sup> Hamman and Wolman,<sup>15</sup> Hyslop-Thompson,<sup>16</sup> Lowenstein,<sup>17</sup> Turton,<sup>18</sup> Bonney,<sup>19</sup> Pottenger,<sup>20</sup> Bandelier,<sup>21</sup> Raw,<sup>22</sup> Dluski,<sup>23</sup> record results which are very much in accord and in favor of the use of tuberculin, even in ambulant cases of pulmonary tuberculosis. Attention is particularly directed to the non-pulmonary forms of tuberculosis—tubercle-bacillus infections, which involve other parts of the body, and with rare exceptions, not involving the lungs, so far as one may determine by physical examination—cases coming under the term of surgical tuberculosis, using the term surgical in its broadest sense to denote invasions of the skin, eye, ear, abdominal organs, and bone. The literature relating to tuberculin therapy in surgical tuberculosis is relatively scanty, for the surgeons as a rule, have been infrequent contributors to the records on immunization and experimental therapy. Much of the convincing literature is hidden away in the excellent monographs on tuberculin by Petruschky,<sup>4</sup> Kohler,<sup>24</sup> Denys,<sup>12</sup> Birnbaum,<sup>25</sup> Beitzke,<sup>26</sup> Daels,<sup>27</sup> E. Klebs,<sup>28</sup> M. Koch,<sup>29</sup> Orth and Rabinowitsch,<sup>30</sup> Luedke,<sup>31</sup> Sahli,<sup>13</sup> Weicker,<sup>8</sup> Bandelier and Roepke,<sup>21</sup> Kohler and Lenzmann,<sup>32</sup> and excellent reports of cases are to be found in articles beginning in 1896 with that of Liebmann<sup>33</sup> and including Nathan Raw's<sup>22</sup> article in 1910. Numerous articles which appeared during these years (1896–1910), will be referred to under the divisions relating to parts affected.

In the *Lancet* for September 17, 1910, p. 885, there is recorded a lengthy discussion by Wright, Latham, Hewlett, Walters, Warner, and Lawson. These observers, with Wright, agree that the proper use of tuberculin, in both surgical and pulmonary cases, is a great step in advance in therapy. Latham<sup>34</sup> concludes that tuberculin is a most potent remedy, which is most efficacious in non-pulmonary forms. Permanent cures for periods over two years in most desperate cases were recorded by him, and he does not hesitate to give tuberculin during pyrexia as high as 105° F. He quotes Ritter, of the Edmundsthal Heilstaette, in Hamburg, as having used tuberculin in minute doses many years ago.

Emery<sup>35</sup> says that its best use is limited to surgical cases, with numerous disappointments and numerous successes—and in conjunction with other methods, tuberculin has its place.

Walters<sup>36</sup> explains that tuberculin is likely to be of service in

two classes of cases: (1) Those in which the slightest exertion causes excessive auto-inoculation (auto-toxosis), and (2) those in which exercise has little immunizing effect.

Nathan Raw<sup>37</sup> has treated with Koch's tuberculin (*humanus*) 110 surgical cases, including adenitis, peritonitis, arthritis, lupus, meningitis, pyonephrosis, cystitis, and prostatitis. In localized forms, most of them of bovine origin, Koch's tuberculin (T. R.) had excellent effect; except in those with encysted pus. In these cases he claims the danger of causing dissemination with resultant blood serum infection. If any tendency to suppuration appears the glands must be opened, but no extensive dissection of glands is indicated in principle and sometimes it leads to generalized tuberculosis. In peritonitis tuberculin has splendid effect, and with operation and drainage many cases remained completely cured. In genito-urinary cases from ten to seventeen injections have an excellent healing effect, when everything else has failed. Raw does not separate "open" and "closed" cases.

These more recent experiences coincide with and are often more enthusiastic than the numerous reports from the larger experiences of Petruschky,<sup>4</sup> Sahli,<sup>13</sup> Goetsch,<sup>5</sup> Denys,<sup>12</sup> Calmette,<sup>38</sup> Beraneck,<sup>39</sup> Rosenbach,<sup>40</sup> and Trudeau;<sup>11</sup> and there is a definite consensus of opinion, among those who have studiously used tuberculin for many years, to the effect that tuberculin therapy is efficacious, and should find a permanent place among methods of treatment.

## PART II. THEORY OF IMMUNIZATION.

It is interesting to refer to Koch's original theory of immunization. Koch<sup>1</sup> found by injecting healthy guinea-pigs with pure cultures of tubercle bacilli that after a period of from ten to fourteen days there developed at the site of the injection a hard nodule, and that after a certain longer period this nodule softened and ulcerated progressively until the animal's death.

EXPERIMENTAL IMMUNITY IN GUINEA-PIGS. Entirely different results were obtained when a tuberculous guinea-pig was so inoculated. The most striking results were obtained in animals which survived infection from four to six weeks. In such animals the inoculation wound scabbed over quickly, but no nodule formed, and on the second and third day a peculiar change appeared at the site of injection, which consisted in a hardness and a dark discoloration spreading about the site for from 1 millimeter to 1 centimeter.

On the fourth day the skin had become necrotic and sloughed off and there remained a flat ulceration, which generally healed quickly and permanently, without infiltration. The guinea-pig infected with tuberculosis had, through the first injection, obtained



such a degree of immunity that the second injection did not take hold.

**USE OF KILLED CULTURES.** Koch found further that the killed pure cultures of tubercle bacilli, triturated in water, when injected in large quantities into healthy guinea-pigs produced only suppuration; and that, on the other hand, in tuberculous guinea-pigs small quantities of the suspended culture caused death within a short while. By methodically repeated use of higher dilutions it was possible to preserve the life of the animal and to bring about a marked improvement.

**ABSORBABLE AND NON-ABSORBABLE PRODUCTS.** It was shown that there was no resorption at the site of the injection and that the suspension remained in the tissue and aroused suppuration. The healing substance must therefore have been thrown out from the bodies of the tubercle bacilli, while the substance which produced suppuration remained behind or was very slowly dissolved. Efforts to extract the healing substance from the bacilli led Koch to the discovery of tuberculin.

Today we know that the substance from the bacilli, acting as antigen, arouses the body tissues to the production of healing substances. Koch thought the healing reaction due to a specific effect upon the tuberculous tissue (bactericidal immunity) resulting in necrosis and healing, and was to be obtained by rapidly increasing the dose. Today we know that from the tuberculin injections, in addition to a local effect upon the focus of infection, there is also immunization against bacterial poison dependent upon bacteriolytic processes which free endotoxins or endoproteins and upon phagocytosis; and that immunity is best obtained by inoculation of small doses slowly increased over a long period of time.

**TYPES OF IMMUNITY AFTER TUBERCULIN INJECTIONS.** According to the knowledge relating to immunization which has accumulated since Koch's time, one must consider two types of artificially acquired active immunity: (1) Antitoxic; (2) antibacterial, *a*, bactericidal; *b*, bacteriolytic (resulting in ant-endotoxic, or ant-endoprotein immunity); *c*, phagocytic, (1) bacteriotropic, (2) opsonic.

**IMMUNE BODIES IN IMMUNE BLOOD.** One may conclude with Spengler,<sup>41</sup> that immune bodies of immune blood in tuberculosis may be agglutinin, precipitin, opsonin, chiefly lysin, and antitoxin (ant-endotoxin), but one cannot agree with him in regard to the mechanism of their formation.

The theory that the action of tuberculin is partly antitoxic (Bandilier and Roepke<sup>21</sup>), is untenable, since the production of soluble toxins by the healthy bacillus has never been proved, and the isolation of endotoxin has not been accomplished; and further, the work of Koch,<sup>1</sup> Maragliano,<sup>42</sup> and Wassermann and Brueck<sup>43</sup> particularly, has proved that immune bodies can be

recovered in the tuberculous focus and also in the blood of man after the tuberculin injections.

**ISOPATHIC IMMUNITY.** Isopathic immunity has been suggested by but few experimenters, among them von Behring,<sup>44</sup> and more recently Webb,<sup>45</sup> who suggested and tried the injection of living bacilli, beginning with a single bacillus, which was carefully obtained by a particularly delicate technique.

**IMMUNIZATION WITH KILLED BACILLI.** Most methods of immunization have been based upon injection of dead bacilli, and it should be recalled that Koch obtained his best results by the injection of bacilli killed by heat; and that Bordet and Gengou,<sup>46</sup> and Dembinski<sup>47</sup> obtained markedly different results between the use of living and dead bacilli, in favor of dead bacilli.

Trudeau,<sup>48</sup> in 1907, discussed antitoxic, antibacterial, and isopathic immunity, and inclined toward the belief in antitoxic and antibacterial immunity in tuberculosis; and in 1909, accepted the antitoxic theory of immunization as particularly appropriate for tuberculosis; and one will find today that most investigators who are familiar with tuberculin immunization believe in the antitoxic—not in the sense of diphtheria antitoxin—and the antibacterial theories, when considering the substances which should be used for injection.\* This may not seem clear, but the day has come when one must consider the possibility of separating products which are particularly poisonous to the human organism and without a marked curative effect, from other substances which are less poisonous and which have a greater curative power. The latter substance or substances should be relatively greater than the former substance or substances in any preparation, such as tuberculin, which is injected for therapy. In 1901 Bordet and Gengou<sup>49</sup> described the complement absorption method for the detection of specific amboceptors. In 1903<sup>46</sup> they reported the experimental production of such specific amboceptors in guinea-pigs injected with living avian cultures and with heated or killed human cultures. Dembinski<sup>47</sup> (1904) concluded that production of amboceptor against the tubercle bacillus depended upon the type of bacillus used (human, avian, bovine), and in 1906, Dembinski's idea was disproved by Gengou, who found that avian bacilli killed by heating at 65° C. for one-half hour or at 100° C. for five minutes produced amboceptor against the various mammalian tubercle bacilli, and that the variation in the amboceptor production depended upon the animal, in that it was less marked in rabbits than in guinea-pigs. Gengou, likewise, found that injection of one type of the acid-fast bacilli, saprophytic or pathogenic, would give

\* The reaction for good or bad is supposed today to be due to the action of a tuberculo-protein upon hypersensitive tissues. For the relation of hypersensitiveness (anaphylaxis) to tuberculin in immunity to tuberculosis, refer to Wolff-Eisner,<sup>64</sup> and Trudeau, Baldwin, and Krause.<sup>66</sup>

amboceptors against nearly all the other mammalian tubercle bacilli, and he recalled the fact that Klemperer had obtained the same results in his earlier experiments upon guinea-pigs. The application of results of the experiments of Bordet, Gengou, and Dembinski to the study of tubercle bacillus infections, with or without tuberculin injections, was first made by Wassermann and Brueck,<sup>43</sup> who concluded that the specific reaction in infectious disease is due to the fact that the focus reacts to the metabolic (*stoffwechsel*) products of its specific antigen, in such small quantities that no marked effect is noted on an organism free from this infection. This was first shown for tuberculin, and diagnostic and therapeutic procedures are based on this specificity. The local (in the diseased tissue) reaction is far more impressive than the general reaction, with rise of temperature.

EXPERIMENTAL STUDIES ON THE WORKING OF TUBERCLE BACILLI PREPARATIONS IN TUBERCULOUS ORGANISMS. Anatomico-pathological changes in the diseased tissue with specific reaction have been much studied. In *resume*: Under injection of tubercle-bacillus preparations, in tuberculous foci there are signs of a flooding with body fluids and an infiltration with the ameboid cells of the blood; consequently a softening and dissolution of the tissue.

Just as old as the studies on the tissue are the investigations for an explanation of the reaction in the diseased tissues. There are many theories. According to Rappoport<sup>50</sup> the tuberculous organism in the sense of von Behring is toxine-hypersensitive.

ADDITIONS-THEORIE. Babes<sup>50</sup> believes that in tuberculous foci tuberculin already exists, and that the tuberculin injected results in summation. Ehrlich's<sup>50</sup> theory, in explanation of the local reaction assumes that the focus, as a bulb, is surrounded by many cell layers. The innermost layer is saturated with tubercle bacillus products (tuberculin), the middle layers are injured through the products, and the outer layer is completely uninfluenced and sound. Injected tuberculin acts neither on the inner saturated, nor on the outer healthy, but on the middle already damaged cell layer. Why the tuberculous focus attracts to itself minimal quantities of a certain tubercle bacillus preparation in the blood stream, and how the entrance of tuberculin into the focus is followed by softening and destruction of tissue, are questions which Wassermann and Brueck attempted to answer.

IMMUNE BODY IN PATIENTS AND ANIMALS NOT INJECTED WITH TUBERCULIN. They reasoned, since lupus cases react to from  $\frac{1}{10}$  up to 1 milligram and the average blood mass is 5 kilos (=5000 c.c.), that if 1 milligram be injected the dilution in the blood is 1 to 5,000,000. Such an amount injected into a lupus focus produces no local reaction. So the entire tuberculin mass by some substance in the focus is drawn out from the circulating blood and then concentrated on the focus. So there must be a

haptophore group (an antituberculin) for the injected tuberculin, in the focus. And one must prove in the tuberculous focus: (1) Presence of the tuberculin-like substance in solution, and (2) reaction products and antibodies for these substances (antituberculin). They employed the Bordet-Gengou complement-fixation method. Rabbit-sheep amboceptor and guinea-pig complement were used.

**ANTITUBERCULIN IN ORGAN EXTRACTS.** Organs or tuberculous portions were rubbed in a mortar with 0.8 per cent. salt solution and 0.5 per cent. carbolic (1 gram of organ to 5 c.c.), shaken twenty-four hours at room temperature and centrifugated. Certain quantities of the clear extract with decreasing amounts of tuberculin (A. T. and B. E.) and  $\frac{1}{10}$  c.c. of pure guinea-pig complement were kept at 37° C. for one hour. Then hemolytic unit was added and kept for from one to two hours at 37° C. and, later, over night on ice. Inhibition in certain tubes proved the presence of antituberculin in tuberculous organ extracts of human lung and glands, and organs from guinea-pigs and cattle.

**ANTITUBERCULIN IN BLOOD SERUM.** They found also antituberculin occasionally in the serum of guinea-pigs and cattle; but in 13 human cases, not handled specifically, in all stages of lung tuberculosis there was no trace of antituberculin in blood serum. Antituberculin in the organs requires the presence of tuberculin. To prove this, they replaced the tuberculin with a good agglutinating serum (from Hoechst) and found tuberculin in tuberculous organ extract, human and mammalian, but not in serum of man, guinea-pig, or cattle. That the two, tuberculin and antituberculin coexist, may in this instance be so.

**IMMUNE BODIES IN PATIENTS OR ANIMALS, OR ANIMALS TREATED WITH TUBERCLE BACILLUS PREPARATIONS.** Antituberculin was found (1) in serum of men injected with tuberculin, after three doses of 1, 5, and 10 milligrams of A. T. No reaction occurred to A. T. and B. E. Before injections, B. E. and A. T. were not active specifically in all cases. No antituberculin was found (2) in normal cases injected with tuberculin. Thus we are concerned with not simple toxic substances, but body substances of the bacillus type. One must not conclude that these tuberculin amboceptors are identical with amboceptors against the tubercle bacillus.

**FEBRILE REACTION.** The febrile reaction depends upon two factors: The first, since it occurs in health following too large a dose, partly non-specific; the second, as a direct result of specific working of tuberculin on the tuberculous tissue, partly specific from soluble digested products being absorbed.

In injected cases, tuberculin and antituberculin combine, and thus the focus is not invaded by tuberculin and there is no marked solution of tissue and no temperature reaction, and finally, there

is no antituberculin in the tuberculous organs and, therefore, no local reaction and no temperature.

Wassermann and Brueck conclude that the explanation of the working of tubercle bacillus preparations in the tuberculous organism may be based on the following: In a large number of tuberculous individuals not treated with specific therapy, there were present in the tuberculous tissues antibodies against the tubercle bacillus preparations. The serum was free from such substances. When one injects such an individual with specific tuberculin preparations, it is clear that the power of the preparation depends upon its avidity for the antibody. Since the last has its location in the tuberculous tissue, in like manner the tubercle bacillus preparation goes to the tuberculous organs. The local reactions, softening, and dissolution of tissue, occur after union of tubercle bacillus preparation and antibody, for complement is attracted, and whenever amboceptor and complement become concentrated, and thus workable (synergic), the pre-existing protein materials are dissolved and digested.

Through union of the tubercle bacillus preparations and antibody, the protein-digesting substance in the blood (namely, complement) is concentrated on the tuberculous tissue, not alone in the form of free digesting substance, so far as it comes from leukocytes through destruction of the last and their solution in the fluids, but also in the form of digestive strength or power which exists in the leukocytes, as shown by the small cell infiltration.

The blunting against tuberculin and the efficacy of its working depend also upon the rapidity and amount of invasion of blood stream by antibody. The best condition for a cure is that there should be antituberculin in focal tissue and little or merely a trace in the blood. The worst is that in which there is little antituberculin in tissue and more in the blood. In healthy man, non-tuberculous, after 1, 5, or 10 milligrams without reaction there was found no antituberculin in serum. This is not so for opsonin.

The specific action of tuberculous tissue occurs because the tuberculins, through their antibodies, are drawn to the tuberculous tissue, and by this process the tissue-softening power of the organism is concentrated in one place. The blunting occurs because the fore-treatment with the tubercle bacillus preparations produces antibodies in the blood.

Marmorek<sup>51</sup> attempted to prove the presence of a "tuberculous" (not tuberculin) substance (toxin?) in the blood serum of tuberculous patients, by complement deviation tests with patients' serum and antituberculous sera from injected animals. This tuberculous substance is a related toxin, and the injection of tuberculin acts as an irritant upon the focus of infection, which calls forth the increased flowing out of toxin and thus the production of antitoxin sufficient for healing. May this not be the same as liberation of endotoxin or endoprotein through bacteriolysis?

**ANAPHYLAXIS.** Emery<sup>35</sup> thinks the tuberculin reaction similar to serum anaphylaxis of guinea-pigs. Tuberculin is, in itself, non-toxic for a normal animal, just as is serum. The tubercle bacilli possibly produce it in small amounts, resulting in anaphylaxis and the wasting and fever may be akin to the phenomenon of Arthus—the reaction of a hypersensitive animal to repeated small doses of a non-toxic substance. If this is the fact, we may regard tuberculin as the true toxin of the disease.

Emery<sup>35</sup> states, however, that the actual toxin and mode of action of the tubercle bacillus tuberculin are unknown. Tuberculin is not a true toxin, for immunized animals are still susceptible to the tubercle bacillus, and one can prepare a serum antitoxic for tuberculin without curative or prophylactic virtues; and tuberculosis may be afebrile. The temperature of phthisis is mainly due to secondary organisms.

Sahli<sup>52</sup> has used Koch's old and new tuberculin, Denys' tuberculin, and chiefly Beraneck's tuberculin and has reported the same. The curing process depends upon desensitizing the organism against the chemical tuberculosis poison. It depends upon making the tissues poison fast (mithridatismus) and is best explained by Maragliano<sup>53</sup> and Wassermann and Brueck,<sup>53</sup> as an increase of the natural ability of the body.

**PHAGOCYtic AND OPSONIC THEORIES.** Metchnikoff<sup>54</sup> years ago proved that living germs are taken up by leukocytes and destroyed, and that phagocytosis usually occurred in mild infections and little or none occurred in fatal infections. He considered this of greatest importance in immunity and thought it should cover the whole field. Baumgarten<sup>54</sup> and Sanarelli<sup>54</sup> noted that recovery occurred when little phagocytosis was found. They described bacteriolysis in collodion bags placed in the peritoneal cavity and, later, others recognized the importance of some substance acting on the bacteria and enhancing phagocytosis—this substance coming from the leukocytes.

Kanthac and Hardy,<sup>54</sup> on frogs, found that eosin cells gave off substances which acted upon the bacteria and hyaline cells. When they injected such bacteria in man, a similar process occurred in which the injurious substances came from polynuclears, which are also phagocytes.

Metchnikoff<sup>54</sup> later described macrocytase from macrophages, which digest cells; and microcytase, from polynuclears, which acts against bacteria.

**THERMOSTABILE OPSONIN FOUND.** Wright was antedated by Denys and Leclef<sup>55</sup> (in 1895), Mennes and Markl,<sup>56</sup> and Neufeld and Rimpau,<sup>57</sup> who found thermostabile opsonin for streptococcus and pneumococcus. Wright elaborated and described independently the opsonin, and strongly advocated the use of vaccines.

Wright<sup>74</sup> states that no disease is more truly a local one: Im-

munity to tubercle bacillus is local rather than general. The main curative agency is due to phagocytosis; but this does not necessarily depend upon the same mechanism noted *in vitro* in the study of opsonins.

The result of tuberculin injection is very complex, and it is at least possible that the curative effect is due to reaction in or near the lesion—very small doses cause a definite local reaction best seen in tubercles of the iris, which are surrounded by a hyperemic zone after 1 milligram of T. R. or B. E.

So far as is known the polynuclear leukocytes act only on the bacilli in the circulating blood. Normal tuberculo-opsonin is completely thermostabile, and the rise in index with or without injections is due to the same. Thermostabile opsonin is never abundant, and not constant. Wright,<sup>54 58</sup> denies the demonstration of any lytic or cidal elements and little is known of any other antibody. No antitoxin is known. Wassermann and others have shown such antibodies in patients after tuberculosis, but their action is unknown.

Mueller<sup>59</sup> says that there is no doubt of the variation in opsonin and in the phagocytic index but this is no explanation of the immunizing reaction. Opsonin does not vary with bacteriolytic power, but seems independent of complementary and bacteriolytic substances, and of agglutinin. This was shown by Wright and Bullock<sup>60</sup> and by Torrey.<sup>61</sup> Serum opsonin is multiple, and varies much with individual types of bacteria; with any type, extremely virulent organisms are not phagocytable, as shown by Hektoen and Rosenow.<sup>62</sup> The opsonin here referred to by Mueller is bacteriotropin, or immunopsonin.

**NORMAL OPSONIN IN CONTRAST TO IMMUNOPSONIN.** He believes that normal opsonin and bacteriolysin are practically identical, in contrast to which immunopsonin (or bacteriotropin) has nothing to do with bacteriolysin. Mueller accepts Wright's classification of bacteria, based upon reaction to the various immune bodies: (1) Bacteria, little affected by opsonins and bactericidal substance, such as cholera and typhus. (2) Bacteria, highly sensitive to opsonin and bacteriolytic substances; coli and dysentery. (3) Bacteria, highly sensitive for opsonin; not so for bacteriolytic substances; *Staphylococcus aureus*, *Micrococcus melitensis*, *pneumococcus*, *Bacillus pestis*. (4) Bacteria, not sensitive to opsonin or to bacteriolytic substances; diphtheria and xerosis. He does not venture to place the tubercle bacillus in any one of these classes.

**ALLERGIE AND IMMUNITY.** Von Pirquet's<sup>63</sup> "allergie" refers to the hypersensitiveness of all the body tissues, and is primarily concerned with the diagnostic reactions. Immunity remains the term for any instance of *allergie* in which a useful hypersensitiveness and increased resistance are attained.

After becoming conversant with the literature, one decides that

the theories for artificial immunization against tuberculosis are individualistic in part, depending upon the line of research which has engaged the attention of the individual investigator; and that the immunizing mechanism follows the several theories combined. This is well presented by Mueller in his lecture on "Infection and Immunity."

**MUELLER'S THEORY.** Mueller<sup>59</sup> states that if the infectious microorganisms invade the body tissues in any way and find the proper physical (osmotic pressure) and chemical (reaction, nourishment) conditions for growth, they begin to multiply. A part of these newly produced germs come in contact with the bactericidal substances already on hand in the locus invaded, and, by these substances, are killed and decomposed. The body substances of the bacilli thus freed, as well as the secretions from them, lure the leukocytes from the tissues and the blood which either through active secretion or through disintegration, provide new bacterio-hostile substances for the tissue fluids, and so cause the renewed killing of the infectious germs. A part of the killed microorganisms are taken up by phagocytes and transported; but living germs, also, having been acted upon by opsonin, can be taken up by the white blood cells and either go to their death or multiply, and after they have destroyed the host cells, go free again.

The toxins produced by the living germs, as well as those going into solution from the bacterial bodies, call forth in the neighborhood of the infected locus more or less extensive anatomico-pathological changes which, according to the kind and intensity of the irritant, show as inflammation, suppuration, necrosis, and tissue proliferation.

With the fluid circulation, the toxic substances pass to the distant organs and produce the changes noted as intoxication signs (ecto- or entotoxosis). Meanwhile, the combat goes forth from the locus of infection. Each succeeding generation of microorganisms is more virulent.

On the other hand, the defensive reaction can persist; the mass of protective stuff or, speaking directly, phagocytosis, is increased. The phenomena of extracellular bacteriolysis takes on a greater significance, although single germs invade the blood stream, to be destroyed or to lodge in the capillaries of some organ.

**TWO FACTORS INFLUENCING OUTCOME.** Mueller states that the final favorable or unfavorable outcome depends upon two different factors: Whether the organism is able to check the bacteriobiosis (bacterial growth) and to destroy pathogenic germs; and, whether it can endure the toxic effect of the metabolic products—the toxin—and the disintegration products—the proteins and endotoxins—of the bacteria. The lethal result may be grounded upon two factors: The relative insufficiency of the detoxicating (apotoxinizing) preparedness after the germs are killed and dissolved; or,



the general failure of the bacteriolytic and phagocytic defences. In the first, the bacteriological examinations of fluids and blood will be negative; in the second, the tissues and blood will be flooded with microorganisms. Between the two forms, toxemia and bacteriemia, all possible transition stages are found.

Mueller agrees with Wassermann and Brueck. The specific tuberculin reaction is due to avidity of the tuberculous focus for union with the injected tuberculin; and the reaction is a concentrated one.

Wolff-Eisner<sup>64</sup> adds that the antituberculous substance possesses the character of a bacteriolytic amboceptor, which, on account of the tubercle-bacillus splitting due to the injected tuberculin, sets free the endotoxin-like (endotoxinoid) poison, and thereby brings about an enhanced toxic reaction.

Wassermann's and Brueck's idea of the tissue lysis due to the digestive action of the bound complement is more comprehensive.

The absence of antituberculin in the blood of the tuberculous individuals who have not been injected with tuberculin and the local antibody production calls for an increase of sessile receptors with no throwing off of these receptors into the blood stream, according to Mueller. (This is not necessarily so; unless one has examined the blood of patients under all conditions of activity and inactivity, which has not been done, for the processes may alternate.)

It is quite possible, in view of Wassermann's and Brueck's and Citron's<sup>65</sup> observations, that the invasion by a secondary microorganism in a pulmonary focus is more likely than in a non-pulmonary focus, for complement action after fixation at site, causing dissolution of tissue must lower resistance to bacteria other than tubercle bacilli.

### PART III. KINDS OF TUBERCULIN

**TUBERCULINS.** The different preparations known as tuberculin are substances, in the media, produced by the tubercle bacilli during growth, substances extracted from the tubercle bacilli, or the bodies of the tubercle bacilli themselves before or after extraction. The injection of tuberculin results in active immunization, and the tuberculins are in no sense serums, as is the popular misconception, for the term serum is continually used even by the medical profession in speaking of the use of tuberculin. The accompanying list by no means exhausts the tuberculins which have been described but contains those most written about and used.\*

\* See Bandelier and Roepke, loc. cit., ref. 21, pp. 140 to 188.

## LIST OF TUBERCULINS.

Variety.	Originator.	Date of introduction.
A. T. or O. T., old tuberculin, original . . . . .	Koch	1890-1891
(T. A. K. or T. A., Denys) . . . . .		1891
Tuberkulocidin . . . . .	Klebs	1896
Antiphthisin . . . . .	Klebs	1896
Tuberkuloprotein . . . . .	Klebs	1896
T. O., Obere Tuberkulin . . . . .	Koch	1897
T. R., rest tuberculin (Neutuberculin T. R.)	Koch	1897
Tuberkuloplasmin . . . . .	Buchner and Hahn	1897
Oxytuberkulin . . . . .	Hirschfelder	1898
Tuberkulol . . . . .	Landmann	1898-1900
B. E., Bacillary Emulsion (Neutuberkulin-Bazillenemulsion) . . . . .	Koch	1901
T. Bk., Tuberkulin . . . . .	Beraneck	1903-1905
Bovine tuberculin (Perlsucht tuberkulin) . . . . .	Spengler (see Note)	1904-05-07
Nastin . . . . .	Deycke and Reshad-Bey	1905
B. F., tuberculin Denys (broth filtrate) . . . . .	Denys	1905
Tuberkulin, CL (Tuberculine Calmette) . . . . .	Calmette	1906
Tuberkulase . . . . .	von Behring	1906
Tulase . . . . .	von Behring	1906
Tulaselaktin . . . . .	von Behring	1906
Watery extract . . . . .	von Ruck	1897-1906
Tuberkulo-cidin-selenin . . . . .	Klebs	1907
Tuberkulonastin . . . . .	Deycke and Reshad-Bey	1907
Tuberculo-albumin . . . . .	Piorkowski	1908
Tuberkulo-sozin . . . . .	Klebs	1908
Tuberkulin, IK . . . . .	Spengler	1908-1909
"Sensitized Bacillus Emulsion" . . . . .	Citrone	1909
Tuberkulin, "weakly toxic" . . . . .	Rosenbach	1910
Endotin, "poison-free" tuberculin . . . . .	Gordon	1910
Tuberculin, "albumose-free" Koch's tuberculin . . . . .	Jochmann and Möller	1910
"Sensitized Bacillus Emulsion," "non-poisonous" . . . . .	Wolff-Eisner	1910

NOTE.—Tuberculins of Carl Spengler, 1904-05-07: (a) A. T. O., original alt Tuberkulin, vakuum Tuberkulin; (b) P. T. O., Perlsucht tuberkulin original, Perlsucht vakuum Tuberkulin; (c) T. B. E., Tuberkelbazillenemulsion, Perlsucht Bazillenemulsion; (d) T. B. V., Tuberkelbazillen Vakzin Perlsucht Bazillenvakzin.

A. T. AND O. T., OLD TUBERCULIN USED NOW CHIEFLY FOR DIAGNOSIS. The old tuberculin of Koch<sup>67</sup> (A. T. or O. T.) is no longer recommended for therapy, but still remains the best preparation for calling forth the various tuberculin reactions for diagnosis. Hunter<sup>68</sup> and Trudeau<sup>69</sup> were among those who early modified the original or produced new tuberculins. Trudeau in 1892 described a broth filtrate which was practically identical with Denys' (1905). Koch<sup>70</sup> was the first to improve upon his original tuberculin (O. T.), which was simply the glycerin broth medium, upon which the bacilli had grown, concentrated to one-tenth its volume, and preserved by the addition of carbolic acid to  $\frac{1}{4}$  per cent. The improvement consisted of the separation of the watery extract, or fluid, in which the bacilli were ground up with a pestle, from the resulting residue which consisted of powdered tubercle bacilli.

T. O. AND T. R. The fluid portion was called Tuberculin "Obere" (T. O.) and the powdered residue Tuberculin "Residuum" or

"Rest" (T. R.). Tuberculin T. R. (tuberculin residue) is prepared from the living, dry, virulent tubercle bacilli, triturated in an agate mortar. The powdered bacilli are suspended in distilled water and centrifugalized, and the supernatant fluid which has the properties of old tuberculin is Obere tuberculin, T. O. The residue is dried, again powdered, emulsified, centrifugalized, and the uniform mass obtained is Tuberculinum residuum (T. R.), which corresponds somewhat to an endotoxin. It is diluted with 20 per cent. to 50 per cent. glycerin, and the addition of carbolic acid is not advised.

DOSAGE BY WEIGHT. There is confusion in regard to dosage, for 1 gram of dried tubercle bacilli is used in preparation of each 100 c.c., so that each cubic centimeter of the remedy contains the material from 10 milligrams of bacilli. But the amount of dry residue is only one-fifth of this amount, so that 1 c.c. of T. R. contains 2 milligrams of solid substance. The dosage adopted concerns the dry residue only, viz., 1 c.c. equals 2 milligrams. This tuberculin should be heated to 0° C. before use.

T. R. OR REST TUBERCULIN (NEW TUBERCULIN). Tuberculinum residuum, T. R., was also called "New Tuberculin," and should not be confused with the more recently described "Bacillus Emulsion," which is also termed "New Tuberculin."

B. E., BACILLUS EMULSION, OR NEW TUBERCULIN. The last, described by Koch<sup>71</sup> in 1901, is a suspension of the bacilli in normal salt solution, thoroughly ground and shaken, so that the fragments of the bacilli are suspended in the fluid, and so prepared that 1 c.c. contains 5 milligrams of the dried powdered bacilli in equal parts of glycerin and water. This is probably the nearest approach attainable to the unmasking of the endotoxins through mechanical means. Several attempts have been made to modify the general toxic action, and to enhance the desired immunizing action through treatment of the bacilli with various chemicals, and by utilizing the combination of the less toxic with the more toxic substances after the isolation of both.

T. BK., TUBERCULIN BERANECK. Such a tuberculin is that of Beraneck,<sup>39</sup> which is the mixture of phosphoric acid extraction of the tubercle bacilli and the concentrated broth in which the bacilli have been grown. This has been described as a mixture of basotoxic and acidotoxic (b. t. + a. t.). Conflicting reports (Sahli<sup>73</sup> and Dluski<sup>72</sup>) are concerned with the use of Beraneck's tuberculin, and Sahli, after years of experience, recommends it as the best preparation. It is supposed to contain ectotoxin and entotoxin, and to be much less toxic than old tuberculin.

TOXICITY OF TUBERCULINS. If one may judge from reactions after injections, Beraneck's preparation is much less toxic than many others. Also, from reactions after injections, one must consider that Denys<sup>73</sup> broth filtrate is most toxic; for reactions

with temperature are not infrequently obtained after the most minute doses of this dilute tuberculin. Denys' broth filtrate (B. F., B. F. H.) is prepared from cultures grown in beef peptone broth with 5 per cent. glycerin. After growth for several weeks, the cold broth is filtered through paper. Phenol to 0.25 per cent. or a little thymol is added to kill any bacilli and as a preservative. The preparation contains the inactive substances, peptone, glycerin, and meat extractives not utilized by the bacteria; the "disassimilation" products of the bacteria, probably ferments, diastases, and albuminoid substances perhaps among them the tuberculo-nuclein of von Behring and, finally, products from the disintegration of dead bacilli. The concentrated filtrate should be kept cold in the dark. The diluted filtrate will not retain its properties more than three or four weeks.

EFFECT UPON TEMPERATURE. The susceptibility of the infected organism to broth filtrate led many to conclude that this preparation is of much value in reducing temperature in febrile cases, and that such can be done will be shown later by reference to Fig. 2, after Denys. That the same effect may be obtained through the Bacillus Emulsion (Koch) will be shown by Figs. 1 and 3. The most recent attempts to prepare more acceptable tuberculins have been along the lines adopted by Beraneck; that is, decreasing the general toxicity and increasing the immunizing power by various means.

TUBERCULIN ROSENBAACH. Rosenbach<sup>40</sup> has prepared a tuberculin by growing tubercle bacilli several weeks old in symbiosis with a fungus (*Tricophyton holosericum album*), grinding up the residue and filtering and mixing this filtrate with the filtered culture medium. He believes that the changes in the complicated proteins, produced through enzyme action, greatly reduce the general toxicity, which is borne out through his experience and by his statement that the initial dose may be as high as 1 to 2 decigrams, and that 1 centigram is a small dose.

COMPARISON OF TUBERCULINS AS TO ADVANTAGE. The preparations of Landmann,<sup>74</sup> von Behring,<sup>75</sup> Hirschfelder,<sup>76</sup> Calmette,<sup>38</sup> Klebs,<sup>77</sup> Piorkowski,<sup>78</sup> Deycke and Reshad-Bey,<sup>79</sup> and von Ruck,<sup>80</sup> have no advantages over and apparently are not so useful, judging from results, as the preparations of Koch, Denys, Beraneck, and possibly Rosenbach. Sigismund<sup>81</sup> has recently compared the potencies of the tuberculins of Landmann, Beraneck, and Koch, and has found Landmann's preparations "D" five times, and "C" ten times more potent than that of the standard (Koch's) tuberculin; and Beraneck's three and three-tenths times weaker than Koch's. This potency refers to the "toxicity" and not necessarily to the immunizing power.

DOUBTFUL VALUE OF BOVINE TUBERCULIN FOR HUMAN THERAPY. Spengler's<sup>82</sup> idea that tuberculin prepared from bovine strains would

prove most efficient, an idea borne out experimentally by the work of Bordet and Gengou, has not found acceptance with those who have had the most experience with tuberculin. Spengler's<sup>83</sup> more recent articles on tuberculin IK, suggest that his later procedure may have value; but from his results, a value not so great as that of the older preparations which have been tried for years.

**TUBERCULIN CL.** Calmette's<sup>38</sup> tuberculin CL is not well known. Strong concentration, less toxicity, production of no fever, with increasing opsonic index, leading to healing, mark this form. Tuberculin CL contains the secretion products from the bacilli in the culture medium, as well as the protoplasmic substances of the bacilli bodies extractable in vacuo with glycerin, precipitable in cold by absolute alcohol, non-dializable with ether, and soluble in physiological salt solution. Its potency is one thousand times that of Koch's old tuberculin.

**TUBERCULOUS IMMUNE-BLOOD IMMUNE-BODY THERAPY OF SPENGLER.** The immune-body therapy (tuberculin IK) of Spengler<sup>83</sup> is not a true passive immunization, but a passive-active one, because the lytic substances dissolve the infectious germs so that the poison through resorption leads to active immunization. This IK is chemically pure, free from albumin and blood pigment, and is the product from immune blood of artificially immunized healthy men and animals. It has a direct antitoxic and lytic bactericidal effect.

Hewlett<sup>85</sup> and Citron<sup>86</sup> suggest that endotoxins after Besredka's method might be more potent; that is, mixing the bacteria with immune serum, and thus sensitizing them before injection, particularly for preparation of prophylactic vaccine.

It is interesting to note that Garbat and Meyer<sup>87</sup> have produced or prepared a typhoid serum after Besredka's method.

**SUMMARY OF BEST PREPARATIONS TODAY.** When we recognize the probability that antitoxic and antibacterial immunization should be considered the most satisfactory, the simpler methods of combining injections of Denys' broth filtrate and bacillus emulsion (Trudeau and Brown), and old tuberculin and the new tuberculin (Petruschky, 1904) recommend themselves as the best to date; particularly, for pulmonary invasion, where the toxic symptoms are more marked than in the surgical conditions.\*

#### PART IV (SECTION 1). ADMINISTRATION.

Administration may be by (1) hypodermic injections, (2) digestive tract (*per orem*), (3) suppositories. For years the hypodermic

\* For recent articles relating to new preparations of nature of tuberculin refer to: Landmann,<sup>84</sup> Hollos,<sup>81</sup> Gordon,<sup>88</sup> Endotin (a poison-free tuberculin). Jochmann und Möllers<sup>89</sup> (Albumose-free tuberculin). Gabrilowitsch,<sup>90</sup> Wolff-Eisner<sup>91</sup> (Sensitized tubercle bacillus emulsion). Meyer.<sup>92</sup>

injections of tuberculin were alone considered. Administration by the digestive tract has been practised and written of by Calmette<sup>93</sup> (1908), Moeller<sup>94</sup> (1908), Hyslop Thomson<sup>95</sup> (1909), and Latham,<sup>34</sup> particularly.

METHOD PER OREM, ENGLISH SCHOOL, LATHAM, WALTERS. Latham still recommends it by mouth, on an empty stomach, early in the morning. The method is most strongly praised by the English school. Walters<sup>96</sup> states that by mouth it may be successfully administered, but often causes pain and nausea, and the effect of the dose is uncertain. Warner finds that administration by mouth is successful, but not suitable for every case. Inman believes that tuberculin so given can be absorbed by the stomach. Lawson supports Latham's oral administration, and by him the needle is rarely employed.

SUPPOSITORIES. Administration by suppositories was attempted by Lissauer.<sup>97</sup>

CHOICE OF CASES FOR TUBERCULIN TREATMENT. In relation to administration, the general pathology of surgical tuberculosis must be considered a moment, for the success in any one instance depends in part upon the selection of cases, or more upon the selection of the proper period during the infection in any one case through which to continue the injections. It may be right, in the one instance, to institute tuberculin therapy before operation and before submitting to hygienic-dietetic treatment; to operate and give tuberculin; to treat surgically alone; to treat hygienically and administer tuberculin; or to combine all these methods. To avoid criticism in regard to tuberculin methods, we have treated, with few exceptions, those cases which have not responded encouragingly to, or have been classed as improper for, surgical treatment, after thorough trial in competent hands.

It is paramount and must be kept continually in mind that the patient, while receiving tuberculin injections, should be under the best conditions of hygiene, diet, and rest obtainable for each case, and that developments such as pus formation and injury to bone should be at once handled surgically; for under such developments we may be dealing with a secondary infection, and the general organism and the focus of infection has to be in a cleansed condition to respond properly and permanently to the tuberculin stimulus.

Petruschky<sup>4</sup> made much of this necessity for toning up each case in order to obtain a proper response, and of properly classifying cases according to their pathogenesis. In 1897, Petruschky<sup>4</sup> described three typical stages, similar to the development of lues without the primary lesion, in the pathogenesis of tuberculosis considered as an early invading and long developing disease.

FIRST STAGE. The primary stage is that of lymph node infection as in the scrofulous type of child, existing in the cervical glands,

in adenoid vegetations, bronchial glands, mesenteric glands; with or without symptoms of poisoning. Those conditions supposed in part to be predisposing, were thought by Petruschky to indicate tuberculous intoxication.

SECOND STAGE. The second stage—that of metastasis development, results in meningeal, pleural, peritoneal, miliary forms, and marks the beginning of processes in skin, bones, joints, and lungs.

THIRD STAGE: "OPEN" TUBERCULOSIS. To the third stage belong the ulcerative pulmonary (phthical) tuberculosis, bone caries, and ulcerative lupus. In this stage the processes are complicated by secondary infection with other microorganisms and constitute the pathogenetic condition of "open" tuberculosis.

"CLOSED" TYPE OF PRIMARY AND SECONDARY STAGE. The primary and secondary stages are the forms of "closed" tuberculosis, in which the tubercle bacilli are not cast off externally, and therefore, imply that the cases are not directly infectious. In studying and classifying our cases of any one anatomical type—glands, eye, kidney, bone—we have strictly adhered to consideration of them as "open" and "closed" in the sense used by Petruschky.

One realizes at once that the "closed" cases, considered as immunizable organisms, present a more favorable prognosis than the "open," unless, perhaps, the latter are to be treated with autogenous (autochthonous) vaccines, or specific antisera for the secondary invasion.

SECONDARY INFECTIONS. There is no doubt, from pathological changes in tissue and from clinical symptoms, that, as a rule, the secondary infection influences unfavorably the course of the disease. According to Petruschky, the claim of Koch that tuberculin (O. T.) is a certain cure against incipient tuberculosis was not far from the truth; suitable for the tuberculin therapy, also, are the "open" cases, in which there is not marked destruction of the organs involved and the general health is relatively good.

NOT GIVEN IN CACHEXIA. Since tuberculin is not a direct-acting substance (as is diphtheria antitoxin) one must expect the organism to possess sufficient strength to react to the toxic material, so that extremely asthenic cases are not suitable for injections. In such individuals first build up strength by good hygiene and food and then use tuberculin. One may add today: Reduce the initial dose in asthenic cases and *do not hesitate to use tuberculin*.

IN FEBRILE CASES: IS TEMPERATURE DUE TO SECONDARY INFECTION? Petruschky<sup>4</sup> also advised against tuberculin in febrile cases, but Denys,<sup>12</sup> Latham,<sup>34</sup> Walters,<sup>36</sup> Inman,<sup>98</sup> and Nathan Raw<sup>37</sup> do not agree with the majority, who hold to Petruschky's belief. With us, as with others, the effect upon temperature has seemed to be dependent upon dosage. Upon those who refuse to inject tuberculin in febrile cases rests the burden of proving that

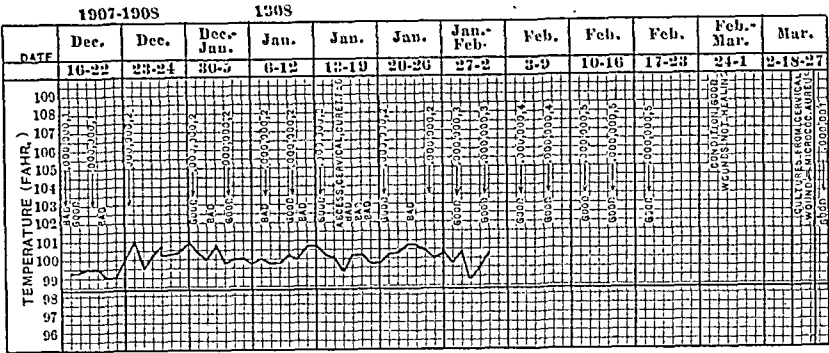


FIG. 1, Section 1.

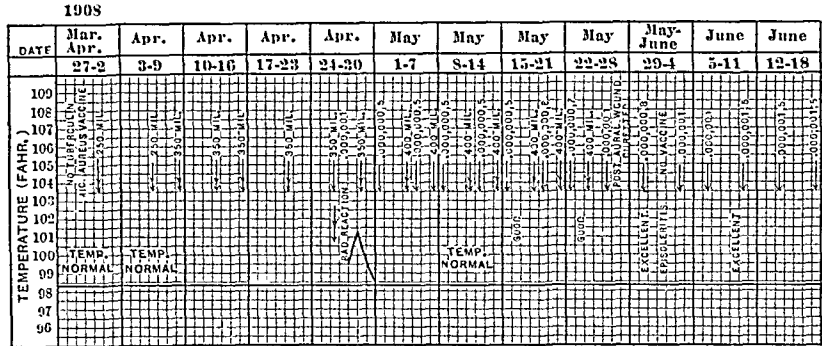


FIG. 1, Section 2.

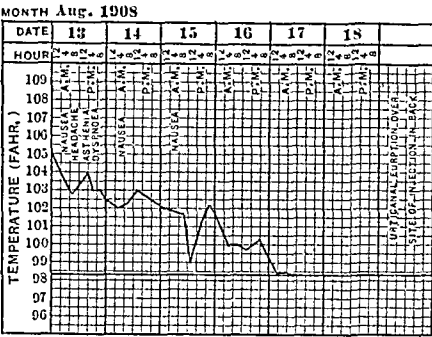


FIG. 1, Section 3.

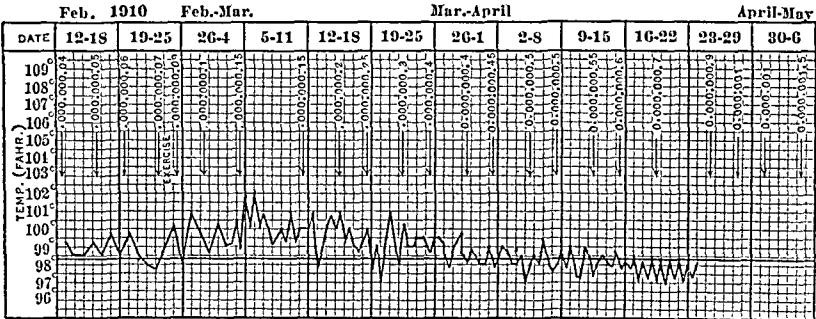


FIG. 1, Section 4.

FIG. 1.—Chart from a case in which temperature persisted although well tuberculinized, until an autogenous vaccine was administered.



the temperature is not often due to secondary microorganisms which may cause the fever, and at the same time would not respond to tuberculin.

**REAL AND APPARENT TUBERCULIN TEMPERATURE.** Fig. 1 shows the chart from a case which shows what may be taken for proof of such a condition, for when well tuberculinized the temperature persisted, but came down after an autogenous vaccine was administered; and later, when wounds were free from staphylococci, the temperature, which had arisen after tuberculinization had worn out, fell rapidly after a few tuberculin injections.



FIG. 2.—Shows lowering of slight temperature and finally reduction in oscillations under tuberculin. (From Denys.)

In Fig. 3 is shown the fall in temperature coincident with improvement, in a case of tuberculous peritonitis. The rise in temperature to  $102^{\circ}$  F. eight days after the last injection followed the Fourth of July, and certainly was not due to the tuberculin injection, but may have been an autotoxic reaction following too violent exercise and excitement, although it was attributed to a digestive disturbance. The child has remained well since that time.

**FEBRILE USAGE.** Walters,<sup>96</sup> in dealing with pulmonary tuberculosis, does not fear tuberculin in highly febrile cases and considers it chiefly or mainly a question of dosage and agrees with Latham in that minute doses will bring down temperature. Lawson<sup>99</sup> thinks that in pyrexia of the pulmonary cases it does not reduce fever and no longer gives it during pyrexia; he makes no reference to surgical cases.

**THE USE OF "SERIES" OF INOCULATIONS.** Petruschky,<sup>4</sup> in 1904, spoke from an experience with many thousand inoculations over a period of thirteen years. Of great importance is Petruschky's statement that most cases, particularly of "open" type, will not go to complete healing with one "kur;" the best term for which, with us, is "series." He recommends often eight to ten series.

After eight to ten weekly injections, a pause of like duration is made and then the "series" is repeated. It is advisable to change the tuberculin preparation; one series being given with old tuberculin, and the others with the new preparations, in order to fortify the body against all the toxic substances of the tubercle bacilli, according to Petruschky.

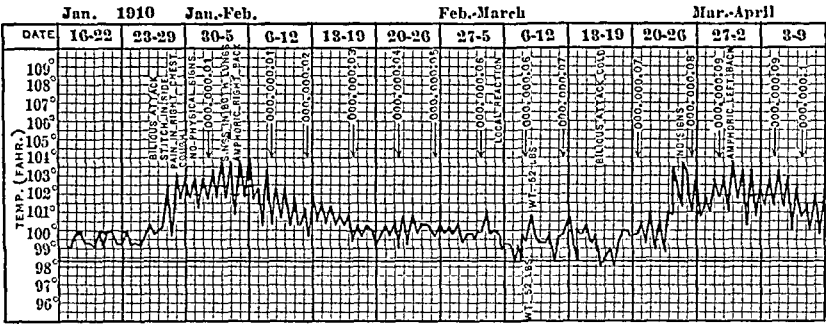


FIG. 3, Section 1.

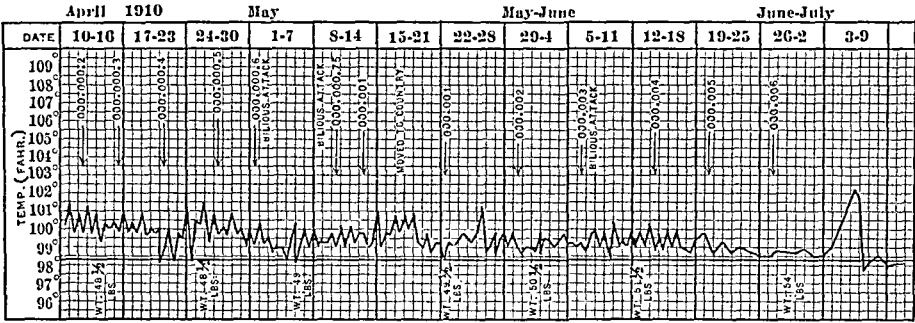


FIG. 3, Section 2.

FIG. 3.—Chart from a case of tuberculous peritonitis treated with tuberculin. The fall of temperature was coincident with improvement.

PART IV (SECTION 2). DILUTION AND DOSAGE AND INTERVAL OF DOSAGE.

DOSAGE OF O. T. AND T. R. Petruschky<sup>4</sup> recommended for a not abnormally sensitive patient, seventeen injections from  $\frac{1}{10}$  milligram to 100 milligrams of old tuberculin (O. T.); 0.1, 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 15, 25, 35, 45, 60, 80, 100, making seventeen doses. For tuberculinum residuum (T. R.) he advises fifteen injections from 0.1 milligram to 100 milligrams; 0.1, 0.3, 1, 2, 3, 5, 5, 7, 10, 15, 25, 35, 45, 60, 80, 100, making fifteen. From experience most investigators consider such doses too high. Between any two injections he allowed at least two free days. After a febrile reaction or pain and tenderness at injection site, the last dose was to be repeated instead of increased, and after a strong

reaction the amount of the last dose was to be reduced and a pause of four to eight days allowed.

DOSAGE B. F. AND B. E. DENYS; TRUDEAU. The system of dilution followed when no other is specified is that, in principle, originally used by Petruschky and modified for smaller doses by Denys. Trudeau was among the first to follow such a method, and it might as well be called Trudeau's as Denys'.

Reference to the following table after Denys<sup>12</sup> will indicate the dilution and dosage.

#### DOSAGE: SERIES OF DILUTIONS.

1.	T-III	=	Bouillon, pure
2.	T-II	=	dilution at tenth
3.	T-I	=	dilution at hundredth
4.	T-0	=	dilution at thousandth
5.	T-0/10	=	dilution at ten thousandth
6.	T-0/100	=	dilution at hundred thousandth
7.	T-0/1000	=	dilution at millionth
8.	T-0/10000	=	dilution at ten millionth

				Pure tuberculin.
0.1 c.c.	T-0/10000	(dilution at ten millionth)	=	0.00000001
0.1 c.c.	T-0/1000	(dilution at millionth)	=	0.0000001
0.1 c.c.	T-0/100	(dilution at hundred thousandth)	=	0.000001
0.1 c.c.	T-0/10	(dilution at ten thousandth)	=	0.00001
0.1 c.c.	T-0	(dilution at thousandth)	=	0.0001
0.1 c.c.	T-I	(dilution at hundredth)	=	0.001
0.1 c.c.	T-II	(dilution at tenth)	=	0.01
0.1 c.c.	T-III	(pure)	=	0.1
				(After Denys.)

This gives eight strengths for dilution, each reduced to one-tenth strength, in terms of cubic centimeters for B. F. and in terms of grams and milligrams for B. E.

The dosage according to Sahli<sup>13</sup> is based upon the method of dilution of Beranek, as shown below in the table.

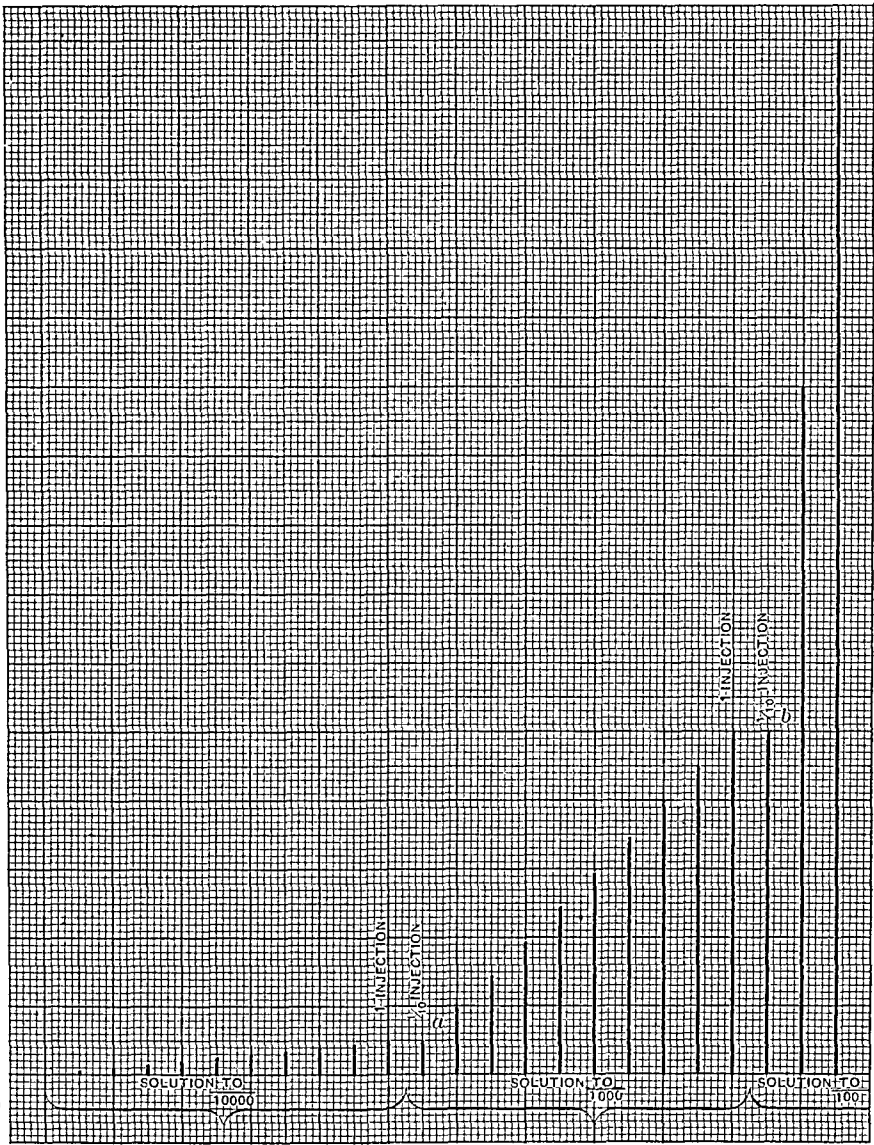
#### Solution of tuberculin, Beranek:

		(Pure tuberculin, Beranek)	
H	= TBk	A/2	= TBk/256
G	= TBk/2	A/4	= TBk/512
F	= TBk/4	A/8	= TBk/1024
E	= TBk/8	A/16	= TBk/2048
D	= TBk/16	A/32	= TBk/4096
C	= TBk/32	A/64	= TBk/8192
B	= TBk/64	A/128	= TBk/16384 usw.
A	= TBk/128		(After Sahli.)

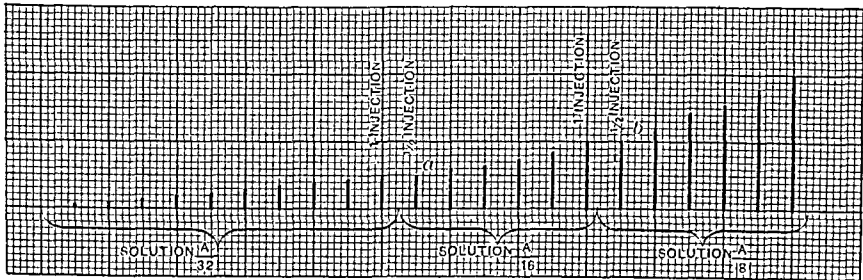
Prepared in thirteen dilutions, each following solution is one-half the strength of the foregoing. Such dilutions permit of a gradual, regular increase in dosage.

When compared to Denys' method, the one usually employed, the difference is striking as shown in Fig. 4.

SAHLI: DENYS. By Denys' method the rate of increment changes with each new dilution on the tenth, twentieth, and



1.



2.

FIG. 4.—(1) Denys' dilution scale. (2) Beraneck's dilution scale. (After Sahli.)

thirtieth doses, which in theory is not so desirable as the regularly graduated increment. Unless some further evidence is brought against it, however, there is no reason for not employing Denys' method.

Brown<sup>100</sup> has proposed an increase by logarithmic scale, based upon dilution in tenths, after Denys' method of dilution, but each injection is varied to the logarithmic scale to meet any desired number of doses per cubic centimeter, as illustrated in the accompanying table.

#### SUGGESTIONS FOR DOSES OF TUBERCULIN

1. These should be from 0.0000001 to 1.2 for B. F. (Never higher than 0.005 or 5 milligrams for B. E.)
2. If there are reactions, begin with a dose of 0.00000001.
3. Continue B. F. and B. E. by giving B. E.  $\frac{1}{200}$  of B. F. dose. (Brown.)
4. Increase according to logarithmic scale:

Doses: 2	3	4	5	6	7	8	9	10	11	12
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
3.2	2.2	1.8	1.6	1.5	1.4	1.3	1.3	1.3	1.2	1.2
10.0	4.7	3.2	2.5	2.2	2.0	1.8	1.7	1.6	1.5	1.5
	10.0	5.6	4.0	3.2	2.7	2.4	2.2	2.0	1.8	1.8
		10.0	6.3	4.7	3.7	3.2	2.8	2.5	2.3	2.2
			10.0	6.8	5.2	4.2	3.6	3.2	2.9	2.6
				10.0	7.2	5.6	4.7	4.0	3.5	3.2
					10.0	7.5	6.0	5.0	4.3	3.8
						10.0	7.7	6.3	5.3	4.7
							10.0	8.0	6.6	5.6
								10.0	8.0	6.8
									10.0	8.3
										10.0

Whatever the method followed for dilution the initial dose is approximately  $\frac{1}{100000}$  milligram of B. E. and T. R., and B. F., for the usual case, with as little as  $\frac{1}{1000000}$  milligram of B. E. and B. F. for the unusual case which reacts generally to the  $\frac{1}{100000}$  milligram. A simpler manner of expression is in terms of  $\frac{1}{10}$  c.c. for a certain dilution, for example: For the initial dose,  $\frac{1}{10}$  c.c. of a dilution of 0.000001 gram (dilution of 1 to  $\frac{1}{100000}$ , or  $\frac{1}{100000000}$  grams), or 5 ciphers (5/1).

Thus the second dose would be 0.2 c.c. of 0.000001, and each succeeding dose would be increased by 0.1 c.c. When for any dilution a dose of 1 c.c. is reached the dilution of 0.00001, or 4 ciphers 1 (4/1), ten times stronger than the preceding, is begun, the first dose of which is equivalent to 1 c.c. of the preceding dilution.

INCREMENT OF DOSAGE, B. F., B. E. Since the increment with a higher dilution is much greater than with the preceding dilution

for each successive dose, one is likely to see general reactions following an injection of a next higher dilution so that it is wise to note carefully the effects of the first three or four injections and to repeat, rather than increase, the dose for the first few injections of the higher dilution.

In some cases the new dilutions should be fivefold and not tenfold the former dilution, and the initial dose 0.2 c.c., equivalent to 1 c.c. of the former dilution.

**FREQUENCY OF DOSAGE, B. F., B. E.** The frequency of injection should not be oftener than twice a week for the smaller doses. Yet this varies with the tuberculin, for Denys recommends the daily injection for a few days at a time, and Sahli also suggests daily injections for Beraneck's tuberculin. For T. R. and B. E. the frequency should be twice a week, for dilutions up to 0.00001 (4/1), and once a week for from 0.00001 (4/1) to 0.0001 (3/1), and once in ten days or two weeks for from 0.0001 (3/1) to 0.001 (2/1).

Emery<sup>35</sup> recognizes three methods of injection: (1) The intensive method: T. R.,  $\frac{1}{10000}$  milligram two or three times a week, increasing to 2 milligrams. The patient is certainly immunized to tuberculin. (2) The opsonic method: T. R., from  $\frac{1}{1000000}$  to  $\frac{1}{10000}$  milligram; the first dose controlled by and the optimum dose and interval determined by the phagocytic index. (3) The use of small doses without opsonic or other control: T. R.,  $\frac{1}{10000}$  milligram once in ten days or once a week.

The total number of injections for a series varies according to different authors with the tuberculin used, but strikes an average between twenty-four and thirty-six in all.

**CALMETTE'S TUBERCULIN (CL).** Calmette's<sup>38</sup> tuberculin (CL) is given as follows: Increasing doses from  $\frac{1}{10000}$  milligram to 1 milligram at twelve-day intervals. On the average a cure follows after twenty-four injections. (288 days = 41 weeks = 10 months.)

**CONTRAINDICATIONS FOR DOSAGE DURING TREATMENT.** A general reaction with temperature within from six to twenty-four hours, rarely twenty-four to forty-eight, should be followed by omission of the next succeeding injection and by reduction of the dosage to one-quarter or one-half of the preceding injection. Local reaction at the injection site with marked swelling, redness of skin, induration beneath skin and tenderness (the classic rubor, dolor, tumor, calor). Finally, with swelling and tenderness of adjacent lymph nodes, repetition should be avoided and the succeeding injection should not be increased, and the interval should be lengthened sufficiently to allow two or three days of comfort after subsidence of the marked local disturbance. Focal reaction (herd reaktion) at the site of infection indicated by discomfort or actual pain, increased redness and local temperature, tenderness, and limitation of motion, when the focus is so located

that it is visible or interferes with free motion of joints, tendons or muscles, must also be avoided, and should be followed by a repetition or maybe even lessening of the last dose, as after a local reaction.

Tuberculin cachexia with loss in weight after high doses, with the tuberculous process apparently in abeyance, is not uncommon, and is a contraindication for continuing injections. When such a condition obtains, the organism should be allowed to rest for a period of three or four months or until the signs and symptoms recur.

**PERIOD OF INCREASED RESISTANCE.** The duration of the increased resistance after a single series was first given by Petruschky as three months for certain cases, and this is readily corroborated by any one over a period of three to four years. The duration varies with the individual, for many patients seem to retain their increased resistance and remain cured for years after a single series, judging from clinical symptoms and subcutaneous tuberculin tests.

**VARIES WITH TUBERCULIN.** The duration of increased resistance seems also to vary with the tuberculin used; for Denys found it persisted for five, twelve, and nineteen months in 3 cases. This increase over Petruschky's period of three months is, in all probability, due to the longer period of inoculation given by Denys.

Petruschky<sup>4</sup> in 1904, reported 2 cures (aged eight and eleven years), of cervical adenitis treated in this manner: The one with five series (etappen) over a period of four years, the other with two series over a period of a year. One would hardly recommend today such rapidly increasing doses, or such large doses ultimately; but attention should be called to Petruschky's lesson in patience and persistence, and the necessity for repeated series of slowly increasing doses over a period of from two to four years—each series of from six to seven months' duration.

**LENGTH OF TIME FOR CURE.** The actual length of time for one series varies considerably with the patient and the type of tuberculin used; but for all it is a question of months and not weeks. For a clinical condition approximating a cure a single series may suffice, and more frequently two and three series are necessary, so that the length of time for a cure may run into years. Wright<sup>58</sup> has recently published a table showing variations from six to thirty-nine months for cures.

Our records show variations from seven to forty months. Trudeau,<sup>101</sup> in 1909, stated that the results to be obtained are: (1) To raise tolerance to tuberculin to the highest for each case. (2) To avoid general and focal reactions; evidence of intolerance. (3) To follow no arbitrary rule or method, but to increase according to the individual tolerance. This result is best obtained by small doses, gradually increased over a long period of time. The initial dose and the rate of increase should be selected to suit each case.

## REVIEWS

---

DUODENAL ULCER. By B. G. A. MOYNIHAN, M.D. (London), F.R.C.S., Senior Assistant Surgeon at Leeds Infirmary, England. Second edition; pp. 486; 78 illustrations. Philadelphia and London: W. B. Saunders Co., 1912.

THE author has conferred much on the surgical world in bringing out his work on *Duodenal Ulcer*. This the second edition is not only considerably enlarged, consisting of 486 pages as against 376 in the old edition, but it also contains a discussion of 115 additional cases operated upon for duodenal ulcer which were not reported in the first edition.

The work considers duodenal ulcer in all its aspects, from the clinical and operative standpoint, as well as from that of the postmortem table.

The writer impresses upon his reader the fact that most "functional" indigestion or "dyspepsia" is nothing but an organic lesion and that "hyperchlorhydria" is duodenal ulcer, a stand that many medical men fail to take.

Much importance is placed by Moynihan on the anamnesis, and he believes that if carefully and intelligently taken it aids greatly in the diagnosis. He also explains his "hunger pain" statement.

The pathology of duodenal ulcer is discussed in detail and the various types taken up and described admirably. Gurling's ulcer, uremic ulcer, ulcer associated with melena neonatorum, jejunal ulcer, carcinomatous, tuberculous, acute, and chronic ulcers all receive their due share of consideration.

The chapter on differential diagnosis and treatment is masterly, and much emphasis is placed on the possibility of there being multiple lesions in any given case, such as duodenal ulcer associated with gallstones, pancreatitis, appendicitis, etc., a very important fact to note at operation.

The surgical technique, the operations, and the factors governing their choice are clearly and concisely stated. Preoperative and postoperative treatment of all cases is described in detail. Especial attention is given to the need of haste, care, and gentleness in the presence of perforation. The various points throughout the work that the author deems important are illustrated by cuts or case histories both of which are complete and satisfying, all unnecessary details, as a rule, being omitted.



Possibly there are too many illustrations of more or less similar specimens, thus giving unnecessary bulk to the book. A few minor typographical errors and the needless repetition word for word of at least one history in two places in the text are the only other adverse criticisms we have to offer.

The work is excellent, well written, clear, and exceedingly instructive, comprising as it does, virtually all that is at present known of duodenal ulcer, its pathology, diagnosis, and treatment.

E. L. E.

---

**SURGERY AND SOCIETY: A TRIBUTE TO LISTERISM.** By C. W. SALEEBY, M.D., F.R.S.E., Fellow of the Obstetrical Society of Edinburgh; formerly Resident Physician Royal Infirmary and Resident Surgeon Maternity Hospital of Edinburgh. Pp. 395. New York: Moffat, Yard & Co., 1912.

"THE motives and purposes of this volume are in part personal, in part, public. The personal motives are gratitude for great benefit lately received from surgery and desire to make some reparation for too hard words spoken of the surgical profession some years ago under stress of intense and honest conviction. The public motives are, to state the case for surgery and, therefore, for science, in modern society; once more to challenge the anti-vivisectionists; to demand the first of what I call the rights of mothers, from my standpoint as a eugenicist; to state the women's share in this most beneficent of human achievements, and to discuss the place and needs of surgery in the new experiments for national control of disease, toward which modern politics is tending."

The paragraph above cited, which is prefixed as a note to this volume, speaks for itself. The book is serious like the author, who with many other zealous men feels his duties in regenerating mankind weigh heavily upon him, and no doubt, sympathizes with the psalmist, who, after explaining that the earth and the inhabitants thereof were dissolved, added "I bear up the pillars of it."

There is no doubt whatever that few intelligent persons will not profit by reading this book. It is interesting in its historical aspects no less than in its statement of present conditions and its prophecy of the future. The descriptions of "Surgery as it Was," of the changes introduced by anesthesia, and of the newer and more rigorous obligations imposed by the discoveries of Pasteur and by all that is connoted in the word Listerism, give graphic pictures of many things which the public ought to know for their own self-protection and that of their families and children, but

of which many even of the most highly educated persons are lamentably ignorant.

Though the author takes the only sensible ground about the vivisection question, his feelings toward the anti-vivisectionists cannot be described as other than intemperate. He recognizes that they are striving for the same ends as is Listerism, but he loses his temper with them because they are dull heads, slow fools, ignorant jackasses (he does not use these words). One might as justly lose his temper with a cow because she could not catch mice, or with an idiot because he could not understand a problem in the differential calculus. "Answer not a fool according to his folly."

The question of microbes, of sepsis, and antisepsis is brought home to every dweller in cities by demonstrating that every large city has only one day's supply of fresh food between it and starvation, and that the *preservation* of food by some means is fast becoming a necessity. "When the fundamental problems of civilization come under serious review by persons who know that they must be solved, and who are thinking not of the next election, but of the next generation, the whole question of what are euphemistically called preservatives in food will have to be attended to; and we shall recognize the necessity for the universal employment of the aseptic instead of the antiseptic method. This will be in wise imitation of the development of surgery, and it will lead us a long way in the direction of a better thing than even aseptic surgery, and that is the disappearance of surgery and surgeons altogether."

The question of pure milk is thus seen to be intimately related to Listerism; and the dependence of surgical tuberculosis on impure milk, which is, we believe, about to be demonstrated scientifically by researches in Scotland where this disease is a veritable scourge, makes not irrational the hope that surgical tuberculosis some day may be as effectually controlled by sanitary measures as is typhoid fever.

The further chapters of the book are concerned with many topics embraced under the general subject of eugenics. Here again the author shows that he is prone to go off at a tangent; but when he keeps to the prescribed circle of his course what he has to say is both entertaining and of great practical interest. The falling birth rate, as he shows, may be combated not by increasing productiveness (which may be difficult or impossible), but by avoidance of puerperal sepsis, thus lowering the risks of motherhood, and saving from death or sterility mothers who shall give birth to still other children. The querulous objection of some that such precautions in childbirth were not necessary in the good old days, he answers by showing that in the good old days ("the *palmy* days," which as Disraeli said "had no *date*") the risks of childbirth were appalling.

Then comes a chapter on Listerism and War; and in this the author points out not only the importance of hygiene in camps, and the part which antisepsis and asepsis have played in decreasing the mortality from wounds in war; but he also proceeds to the matter of recruiting soldiers and to the difficulty which is experienced in some countries in obtaining physically fit recruits—all because Listerism as applied to childbirth, to the slums, to the public-school system, etc., has not been understood by the politician.

This is but half of the book; but the space allotted for review has already been exceeded, and we trust that the character of the volume has been indicated, and that there are many who will want to read it to the end. It is worth it.

A. P. C. A.

A TREATISE ON TUMORS. FOR THE USE OF PHYSICIANS AND SURGEONS. BY ARTHUR E. HERTZLER, M.D., Assistant Professor of Surgery in the University of Kansas. Pp. 728; 538 illustrations, and 8 plates. Philadelphia and New York: Lea & Febiger, 1912.

THE book is divided into three parts. The first part deals with the general biology of tumors, including discussions of the nature, classification, structure, growth, metastasis, etiology, and other important features. The second part consists of eighteen chapters dealing with the pathology of the special forms of benign and malignant tumors. This part is broadly pathological in character, but the pathological features are made subservient to the more dominant clinical phases. The third part deals with the regional consideration of tumors and is essentially clinical in character, making frequent reference, however, to the more purely scientific material of the second part. Twenty-six chapters comprise the third part, four of which are on the female genital tract, one entire chapter being devoted to carcinoma of the uterus. The book is profusely illustrated with drawings and photographs of clinical appearance, gross morbid anatomy, and pathological histology of tumors, in addition to which there are several illustrations of steps in operations indicated in the treatment. The binding is excellent, the paper heavy and glossed, and the type large and clear, divisions of the text being indicated by heavy-faced type and italics. The index is not so complete as might be desirable, there being no mention of several important conditions, notable among them being epithelioma. This is not a matter of nomenclature for the term appears in the text in various places.

From the point of view of the pathologist the book is fairly complete. It adds little if anything to the present conceptions of the etiology and general biology of tumors. Exactness of termin-

ology is not strictly adhered to, but this feature does not serve to diminish the clarity of the subject matter. The classification is simple and clear, but not sufficiently comprehensive in the subdivisions. There is too little stress laid on the subdivision of the epithelial tumors and the consideration of the various types of malignant epithelial tumors is incomplete, in so far as the histological types are concerned. In this group the important benign cystic epithelioma has not been placed, nor is it found in the index. It seems unfortunate that the "vast field of experimental oncology has been entirely omitted," for there are undoubtedly many facts that have been learned that are adaptable to a broad conception of tumor biology in its relation both to the experimental worker and the practitioner. This is especially true of transmissibility, local and general immunity, and heredity. The illustrations in this division tend to be sketchy in the histological details, as for example, Figs. 15, 17, 31. There is little attention given to the finer study of highly magnified preparations.

The regional consideration of tumors presents the work in a thoroughly authoritative fashion and is worthy of the highest praise. Both physician and surgeon will find here much of interest and instruction, for there are presented in very clear fashion the pathology, diagnosis, and treatment of the various tumors found in the given region. A clear idea is presented as to the relative frequency of the tumors considered, the differential diagnosis is discussed sufficiently and a very detailed description of the modes of treatment indicated. Important operations are described and illustrated and some of the plates, notably that showing the lymphatics of the neck are exceptionally good. The illustrations descriptive of the clinical phases of the tumors are excellent and are splendidly correlated with gross morbid anatomical and histological photographs and drawings. The literature in this division of the book has been brought up to date much more carefully than that of the part on tumors in general.

On the whole the book may be said to be of value to the laboratory man chiefly as it brings him in touch with the views of the practical surgeon; but for the general practitioner, the student of surgical pathology, the active surgeon, it must prove of great interest and worth.

H. T. K.

---

LABORATORY MANUAL OF PHYSIOLOGY. By FREDERICK C. BUSCH, B.S., M.D. Second edition; pp. 212; 46 illustrations. New York: William Wood & Co., 1911.

THERE is no field in the medical sciences in which a good book is so necessary as in that of practical physiology. The unsettled

and different attitudes of the various teachers of this branch is difficult to meet. What is considered of great importance by one is given a subsidiary position by another. Therefore the fact that this book, under these difficulties, has reached its second edition justifies attention and favorable consideration. The author covers the whole subject in a general way, starting with experiments of a fundamental nature and extending these to include phenomena of an applied nature. His purpose is to give a fundamental knowledge of the subject to the general student, and at the same time to make the exercises have a practical value to the student of medicine. Although one may wish for a greater and more thorough consideration of the latter side of the subject, nevertheless it is impossible in many laboratories with their limited available equipment. The author has succeeded in giving us a book that can be generally used. The instruments with which the student must become acquainted are described in a simple and lucid manner, and the diagrams are valuable. The book is sufficiently illustrated, and the exercises clearly described. In all, the book is a valuable addition to those already existing and has many advantages.

E. L.

---

**PATHOLOGISCHE ANATOMIE: EIN LEHRBUCH FÜR STUDIERENDE UND AERZTE.** Herausgegeben von L. ASCHOFF. Second Edition. Volume I: General Etiology and Pathology. Pp. 778; 419 illustrations, many of which are colored. Volume II: Special Pathology. Pp. 997; 655 illustrations, many in colors, and 1 lithographed plate. Jena: Gustav Fischer, 1911.

THE fact that this book in the short space of two years appears in a second edition is sufficient evidence of its wide popularity. Its merit is unquestionable and its scope is so great that a detailed review seems advisable.

The extensive alterations found in text, arrangement, and illustration make for vast improvement in the work and in its present form the book is practically a new entrant in a field where its excellence alone is sufficient reason for its being. Assuming that the reader has some familiarity with the first edition, it is sufficient to point out the principal changes made in the second edition.

The chapter on exogenous causes of disease, which in the first edition was the last work of Albrecht, has been somewhat rearranged and enlarged by R. Rössle, the enlargement being most noticeable in the latter's comprehensive discussion of heredity and heritable conditions. Askanazy, in rewriting the chapter on exogenous causes of disease, has retained the form of his original contribution, but has added numerous valuable illustrations, the colored drawings

of the ova of many of the metazoan parasites being of especial value in rendering the text additionally instructive. Following these chapters an entirely new chapter by Rössle, on the general pathology of the cell, has been inserted. This is a brief but intensely thoughtful consideration of the morphological, physical, and chemical organization of the cell in its normal and pathological conditions; it serves an extremely useful purpose in elucidating the retrogressive cell phenomena. Schwalbe's chapter on malformations and monsters has been altered so little as to need no comment.

Gierke's chapter on metabolism has been increased in text and illustration, and the writer presents his subject with increasing breadth of view. As in the first edition, however, he permits the pathological conceptions to outweigh all others, and waving aside the wider considerations of metabolism as a complex process in the entire organism, deals chiefly with the morphological changes which result from altered nutrition and metabolism of the individual cell or organ.

Dietrich's chapter on circulation has been enlarged by an increased elaborateness of discussion of the circulation in its general aspect, of the disturbances of lymphatic circulation, and of embolism and metastasis. He clings to Cohnheim's conception of end arteries, and continues to accept the old Weigert distinction between hemorrhagic and anemic infarction.

In the first edition Kretz presented the subject of immunity in eight pages. He has rewritten and enlarged this chapter so that the subject matter, much of which is printed in fine type, now occupies thirty-one pages. Brief as is its present form, the chapter gives a clear discussion of the condition of infection, the pathogenesis of infectious diseases, and the nature of immunity. The descriptive sections on serum therapy, bacteriolysis, agglutination, precipitation, anaphylaxis (hypersusceptibility), cytotoxins, and phagocytosis (including opsonins) individually are good, but, as indicated, are arranged in an illogical and unnecessarily confusing sequence. Following these sections, the theory of immunity receives conventional discussion and is illustrated with the usual diagrams of Ehrlich's side-chain theory.

Lubarsch's chapter on inflammation can be dismissed with the simple statement that only slight alterations have been made, the article preserving its original clearness, authority, and breadth of view.

Borst, in his chapter on pathological growth, has considerably elaborated the discussion of metaplasia, and has written a section on transplantation, which is so much more complete and comprehensive than that of the first edition that it essentially is a new presentation. The same writer also has revised his chapter on tumors, including in the new edition an excellent discussion of

experimental work on tumors and a splendid *resume* of the present knowledge of the nature of tumors, which has been acquired by experimental research. Except for a slight change in the position of adamantinoma, the classification remains the same as in the old edition.

The sense of proportion and balance displayed in the book is splendidly maintained throughout, the only possible exception to this statement being the brevity of the chapter on immunity. It would seem that the rapid growth and increasing importance of this subject demands more attention both from pathologist and bacteriologist than even the enlarged chapter by Kretz, gives it. Granting this, however, it will be seen that this edition lays new claim to the position which Aschoff's book, from its first appearance, took as one of the leading German works in general pathology. Its excellent artizanship, its logical arrangement, its judicious illustration, its careful, clear, and painstaking treatment of the wide variety of subjects necessary in such a work, make its recommendation a duty and pleasure.

In addition to an enlargement and revision quite in keeping with that seen in the volume on general pathology, the volume on special pathology shows numerous changes in arrangement. In the present form of the book the chapters on nervous system, urinary apparatus, and genitalia follow one another in the order named, but appear between the chapters on respiration and gastro-intestinal tract; the chapter on the thymus body is retained, but the hypophysis, which was discussed in an appendix to the chapter on nervous diseases, now is included in the chapter on glands of internal secretion. All the chapters have a bibliography appended, a feature much missed in the first edition.

Aschoff has rewritten and enlarged his chapter on heart and pericardium, has elaborated the discussion on pathological physiology of the heart, and now gives a clear but brief exposition of the alterations in rhythm and association which follow disturbances of the cardiac transmission tracts. Benda's chapter on the vessels shows the beneficial effect of much careful rewriting, rearrangement, and additional illustration, and is advantageously enlarged by new and complete sections on veins and lymphatic vessels. Schridde, in the chapter on the blood-forming organs, has enlarged the sections on Hodgkin's disease and on the "myeloses." It is gratifying to see his increasing appreciation of the interrelation between the outspoken leukemias and similar aleukemic conditions. Naegli's chapter on the blood remains much as it appeared in the first edition, except for elaboration of the sections on the various forms of anemia and leukemia.

O. Naegeli's chapter on the thymus is enlarged, and the subject is presented clearly and concisely, but his personal views are emphasized even more dogmatically than in the older edition.

M. B. Schmidt has retained much of the form and text of his interesting and well-written chapter on the organs of motion (bones, joints, muscles, etc.) and has added an instructive section on the permanent alterations in the skeleton resulting from congenital and acquired pathological conditions.

Beitzke's chapter on the organs of respiration shows a more complete consideration of the diseases of the bronchi and a more elaborate discussion of the inflammatory processes in the lungs than appeared in the first edition.

The changes in P. Ernst's chapter on the nervous system are slight and hardly worthy of description.

Aschoff, in the chapter on the urinary apparatus, now divides chronic kidney affections into three instead of two groups—chronic tubulo-glomerular nephritis, chronic regenerative nephritis, and chronic kidney alteration the result of altered circulatory conditions.

M. Simmonds, in rewriting and enlarging his chapter on the male genitalia, has added several new illustrations, and has included in the text a new and valuable section on the pathology of the male urethra. Aschoff has rewritten the chapter on female genitalia so as to enlarge it and make it of distinctly greater value.

Almost certainly the most gratifying change is found in the chapter on the gastro-intestinal tract. In the first edition this was covered in a somewhat perfunctory fashion by Bernh. Fischer, but in the second edition has been taken over by Aschoff. The latter, although adhering to the original plan of Fischer, has entirely rewritten and greatly elaborated all the sections; he has added a section on hernia, and has made the chapter a splendidly written, well illustrated exposition of the pathology of this system. C. Sternberg has made very little change in his chapter on liver, bile passages, and pancreas.

Von Gierke, in the chapter on glands of internal secretion, markedly improves his chapter by a greater elaborateness of discussion of the normal and pathological physiology of the various glands.

Jores, in the chapter on skin, has made only minor changes in text and nomenclature.

It will readily be seen that the entire book has received alterations which distinctly increase its value. It deserves the same high praise that is bestowed on the volume on general pathology. It is difficult to understand the unfortunate sequence of chapters which has been mentioned above; and there is no clear reason why the thymus should not be included with the ductless glands, especially when one observes the statement of Naegeli himself that this gland is not lymphatic in character, nor does it have any blood-forming function, being in his opinion a gland purely of internal secretion. Putting aside these more or less academic considerations, the fact remains that the book is well balanced and well



written, it shows an admirable attempt to break away from purely morphological descriptions, shows a spirit of deep philosophy, is a safe guide and authoritative text-book, and in common with the volume on general pathology should continue to hold an extremely high place in the scientific literature of the world. H. T. K.

---

DIE STÖRUNGEN DES VERDAUUNGSAPPARATES ALS URSACHE UND FOLGE ANDERER ERKRANKUNGEN (THE DISTURBANCES OF THE DIGESTIVE APPARATUS AS THE CAUSE AND CONSEQUENCE OF OTHER DISEASES). By DR. VON HANS HERZ, in Breslau. Second edition. Part I. The Blood, Metabolic and Constitutional Diseases in their Relation to the Digestive Apparatus. Pp. 218. Berlin: S. Karger, 1912.

WITH this volume begins the publication of the second edition of Herz's comprehensive correlative work on the disturbances of digestion, and the statement is made on the cover of Part I that the further numbers will appear in quick sequence. As far as the writer is aware, there have been no English translations of this work, the first edition of which appeared in 1898.

To wide readers of foreign literature or to European workers it doubtless needs no introduction, but to the American medical public the work is probably but little known.

To pass final judgment upon the present edition as a whole from the first section now at hand, would be premature, but a review of Part I suggests that no radical departure is to be made in this edition from the plan and scope of its predecessor. The title of the work reveals what an almost limitless field Herz has attempted to cover, and how nearly impossible of success such an effort must be in our present state of knowledge. That a single author should compass the multitudinous relations implied is bold enough, but is, perhaps, less remarkable than that he should be able to present them with brevity. It is plain that this could be accomplished only by necessary sacrifices here and there, but Herz has succeeded, nevertheless, in presenting an enormous array of curious, commonplace, and rare facts of a practical and very real interest.

The plan of the work consists in presenting and considering at length, under their respective headings of the various diseases of other organs, those disturbances of digestion which may occur as the causes, complications, or sequelæ of these conditions. In his discussion of these factors, the author presents the views of leading workers in a given line, less by a statistical summary of what has been done than by a rather happy personal style of exposition which holds the readers' attention. There is given here, of course, much play for individual opinion, of which Herz stands in no

lack, but he seems to have kept a dispassionate outlook in the midst of much controversial evidence, frequently leaving the issue frankly undecided. In other cases, however, he does not hesitate to offer conclusions as when, under gout, he states that until further evidence is forthcoming, we can in general, regard digestive disturbances in this condition as an expression of the gout itself.

The advance of medicine since the publication of the last edition of this work has been so considerable as to necessitate, evidently, not only the rewriting of most parts, but also the composition of many new one, evidence of which is clear in the table of contents and the rearrangement of its sections. Tetany, for example, has come in for a share of attention which the activity of workers in that line has of late years drawn upon it. In a consideration of its etiological factors, Herz takes occasion here, as elsewhere, to indicate his own attitude. He leans away from the view which would make gastro-intestinal toxins in the circulating blood factors of direct injury to the parathyroid glands, and espouses instead the interesting but fancifully elaborated hypothesis of which Falta, Eppinger, and Rudinger are the sponsors.

The field of usefulness of a work such as this lies, of course, in many directions, but it must extend chiefly to the clinician who concerns himself with a philosophical view of medicine or the more abstract research worker who may enter the clinical realm. The book is not one from which the practical physician may expect much help, except in the study of obstruse problems within its sphere, but it should be of much interest to any intelligent reader of medicine, and a store-house of information to the clinical investigator.

The paper on which the work is printed is rather heavy, but the type, as in most German texts, is excellent. A fairly extensive bibliography accompanies Part I.

R. P.

---

CESAREAN SECTION IN GREAT BRITAIN AND IRELAND. By ARMAND ROUTH, M.D., F.R.C.P. Obstetric Physician to Charing Cross Hospital, London; and Consulting Physician to Samaritan Free Hospital for Women, London, etc. Pp. 233. London: Sherratt & Hughes, 1911.

THIS book is the enlargement of a report read at the international Congress in St. Petersburg, 1910, and contains tables of 1282 cases of Cesarean section by over 100 British obstetricians and gynecologists living on June 1, 1910. It is designed to present a complete statement of British work done in Cesarean section. Cases of hysterotomy and hysterectomy performed before fetal viability, and cases of ruptured uterus have been excluded.

Routh introduces before his tables a historical sketch of the various operations which preceded Cesarean section, and also the modern operations which compete with it.

In treating of the history of Cesarean section in Great Britain, he quotes Playfair's statement in 1866 that the mortality was then 89 per cent. The mortality of Cesarean section has steadily diminished from 38 per cent. in 1891 and 1896; 20 per cent. in 1902; about 12 per cent. in 1904, until at the time of writing the operation has scarcely any morbidity, and a mortality under favorable conditions of 2.9 per cent.

In 1906, 90 cases for contracted pelvis are reported with a mortality of 2.2 per cent.; in 1908, 154 cases with a mortality of 4.5 per cent.

Routh brings up the interesting question of Cesarean section in septic cases, and draws attention to the familiar fact that repeated examinations and efforts to deliver with forceps increase the mortality three-fold. Likewise the rupture of the membranes before operations increases the mortality nearly five times.

He draws attention to Maxwell's recommendation that the amniotic cavity be irrigated with normal salt solution or boric acid solution, at a temperature of 100° F. before Cesarean section is performed. This may be accomplished by passing a soft metal, pliable tube into the uterus.

Where the parturient canal is probably infected, and the fetal heart weak, or the child deformed or injured, craniotomy with intrauterine irrigation is indicated; where the uterus is evidently infected, hysterectomy with intraperitoneal treatment of the stump. Thus in 216 cases infected before operation, the maternal mortality was 27.7 per cent. with the classic Cesarean section; while in 14 cases infected, treated by hysterectomy with intraperitoneal treatment of the stump, there was no maternal mortality.

In contracted pelvis, British obstetricians induce labor at the thirty-fifth week for moderate contraction, with the fetus of proportionate size. If the patient is first seen at full term or labor, with no attempts to deliver, conservative section would be chosen, and in infected cases hysterectomy.

In pregnancy complicated by fibroids the patient should go to term, with section if required. In cancer, patients seen early, should have total hysterectomy, if the case is favorable for operation. If unfavorable, the patient should go as nearly as possible to full term and be delivered by section.

In ovarian tumors complicating pregnancy, it is safest to remove the tumor as early as possible. In cases seen at labor, if the tumor is abdominal, vaginal delivery should be practised with ovariectomy later. If conditions are unfavorable, removal of the tumor and section are best.

Where other pelvic tumors, retroflexion of the uterus, or stenosis are present, section has a legitimate field.

It is thought that in concealed accidental hemorrhage abdominal Cesarean section may be done in the interest of the mother. In placenta prævia, section is limited to rigid undilatable cervix, with mother and child in good condition. In eclampsia, with the patient getting steadily worse and the cervix undilatable, abdominal Cesarean section may be employed.

Vaginal Cesarean section is not a favorite operation in Great Britain.

At the time of writing, it is estimated that Cesarean section by all operators, from all indications in the United Kingdom, has a maternal mortality of 8.1 per cent. In contracted pelves the mortality with all operators was 6.1 per cent., and when favorable cases were selected was 2.9 per cent.

This interesting and valuable collection of cases will prove of great service to obstetricians throughout the world in determining the true place for the important operation of delivery by abdominal section.

E. P. D.

---

A MOTHER'S GUIDE. A MANUAL FOR THE GUIDANCE OF MOTHERS AND NURSES. BY FRANCIS TWEDELL, M.D., Alumnus Bellevue Hospital, New York; Fellow of the New York Academy of Medicine; Assistant Physician to the Babies' Hospital Dispensary, New York. Pp. 183; 10 illustrations. New York: James T. Dougherty, 1911.

THE author's statement, in his preface, that he aims "to give simple, clear, and complete directions, especially as regards nursing and artificial feeding of infants, and disorders of digestion," is well borne out by a perusal of his book. This little work will undoubtedly prove to be a great help to physician, nurse, and mother.

The physician will find it useful as a source of reference to which the mother can be directed for specific information as to how to carry out his orders, such as for pasteurization, sterilization, peptonization of milk, preparation of whey, barley water, beef juice, etc. To the nurse it will be a ready reference book when memory fails.

An intelligent mother, who grasps the thought of the book and so acquires a rational outlook on the problems of infant life, will be well repaid for the time spent in its study. As a guide to how to keep a healthy baby well it leaves nothing to be desired.

The advisability of including the section on acute infections is doubtful, especially as treatment is outlined. The symptoms of graver import are, however, described and if the frequent admonition to call in the family physician is not disregarded, while this treatment is tried, it may serve a useful purpose.

A. A. H.

**OPHTHALMIC MYOLOGY. A SYSTEMATIC TREATISE ON THE OCULAR MUSCLES.** By G. C. SAVAGE, M.D., Professor of Ophthalmology (Defects of the Eye) in the Medical Department of Vanderbilt University. Second edition; pp. 685; 84 illustrations and 6 plates. Nashville: Published by the Author; printed by McQuiddy Printing Company, 1911.

As the law of monocular and binocular rest and motion, as also the law of direction, is based upon the recognition of the true locations of the posterior and anterior poles of the eye, the author insists that Helmholtz's work is vitiated by two fundamental errors: (1) In not taking the centre of the macula as the posterior pole, and (2), in holding that visual lines are axial rays instead of prolonged radii of retinal curvature. He also thinks that Listing's law is not true, but "should be forgotten in the interest of truth." The writer posits a number of innervation centres, not upon the basis of anatomical localization, which he considers necessary to explain the phenomena of ocular movements.

In the practical portion of the work adequate space and consideration is given to the various anomalies of the ocular muscles. Cyclophoria, which is in large measure peculiarly the writer's own domain, is perhaps more fully treated than in any other work dealing with this subject. Numerous apposite clinical cases are cited in illustration of the principles laid down. Among the former, it may be worth while to call attention to the report of a case in which an eye with good vision was enucleated, but not by the author, to relieve severe nervous symptoms caused by what was considered hopeless muscle imbalance. The operation is said to have cured the patient—a truce to comments!

T. B. S.

---

**MANUAL OF PRACTICAL PHYSIOLOGY.** By JOHN C. HEMMETER, M.D., Ph.D., LL.D. Pp. 223; 55 illustrations. Philadelphia: P. B. Blakeston's Son & Co., 1912.

THE practical physiology of Hemmeter is the product of the long experience of the teacher and no doubt, in the hands of his students, is of great value. The instruments described are in a large measure those of Porter, from whom he liberally contributes in describing them. He takes up in an elementary manner, muscle and electrophysiology. In like manner he considers blood and circulation. Respiration receives scant attention as does vision and digestion. The internal secretions, however, are given considerable space and the chapter devoted to this subject is very satisfactory. Immunity is also referred to. The text is clearly written in simple language which, no doubt, can be readily understood by the student.

E. L.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**The Successful Inoculation of Blood, Blood Serum, and Sperm of Syphilitics into Rabbits.**—P. UHLENHUTH and P. MULZER (*Berl. klin. Woch.*, 1912, xlix, 152) have succeeded in inoculating rabbits with the blood, blood serum, and sperm of syphilitics. The defibrinated blood of a woman with secondary lues (only a few papules on the buttocks) was obtained from an arm vein. On dark field examination, no spirochetes could be demonstrated. Into the testicles of each of three rabbits, 2 c.c. of blood was injected. All three animals developed a syphilitic orchitis with enormous numbers of active spirochetes in the lesions. The first lesion appeared just eight weeks after inoculation. From a man with florid syphilis, a recurrence following salvarsan treatment, defibrinated blood and blood serum were obtained and were similarly injected into the testicles of rabbits. From the same patient sperm was secured by manual friction. The penis and glans were free from visible lesions. They were thoroughly cleansed and the sperm, received in a sterile Petri dish, was immediately diluted with about one-half volume of lukewarm salt solution. One cubic centimeter of this mixture was injected into each testicle of three rabbits. The sperm showed actively motile spermatozoa, no red blood corpuscles or pus cells. Neither blood, blood serum, nor sperm showed spirochetes on examination with dark field illumination. Blood and blood serum each gave two positive inoculations out of three trials, while with sperm all three animals inoculated developed syphilitic orchitis. Uhlenhuth and Mulzer suggest the bearing of these experiments on hereditary lues and on the diagnosis of obscure cases with negative Wassermann reaction. The inoculation method opens wide possibilities which are being investigated by Uhlenhuth and Mulzer.

**An Epidemic of Sore Throat Due to a Peculiar Streptococcus.**—D. J. DAVIS and E. C. ROSENOW (*Jour. Amer. Med. Assoc.*, 1912, lviii, 773) state that during the last three months in Chicago, there has been an epidemic of sore throat characterized by unusual severity, and with complications strikingly different from those of other years. A streptococcus with certain features is found in practically all cases. The attack begins suddenly with or without chill. Fever and constitutional symptoms are out of all proportion to the local involvement. The throat presents a diffuse redness. The tonsils are always infected, the crypts filled with exudate. A grayish membrane may spread over a large part of the tonsil with only occasional ulceration. The acute symptoms often subside in a few days. But at the end of a week, the patient may suddenly become worse with a clinical picture suggesting septicemia. The cervical glands may become very large, but usually do not suppurate. Otitis media is frequent. Empyema, erysipelas, meningitis, etc., are found as complications, most often in the group of cases with little glandular involvement but marked constitutional reaction. Blood cultures are usually negative. A pure streptococcus can be grown in practically all cases, from the tonsils and secondary lesions indicated; it is Gram-positive, capsulated, occurring in short chains and pairs. Culturally it appears to occupy a position between *Streptococcus pyogenes* and *mucosus capsulatus*. It is not the pneumococcus. Passage through animals, to all of which the organism is highly virulent, increases the capsular substance strikingly. From this characteristic, and from the fact that the capsule is lost on artificial media, Davis and Rosenow suggest that the capsule and high virulence are the results of frequent human passage, which may explain the unusual tendency to complications, and the general severity of the disease.

**Pericarditis in Bright's Disease; Its Relation to Nitrogen Retention.**—F. WIDAL and A. WEILL (*Jour. Urologie*, 1912, i, 177) observe that pericarditis has long been recognized as a complication of chronic nephritis. Bright believed its frequency due to chemical alteration of the blood. A review of more recent literature shows varying opinions as to its cause. Widal and Weill have studied 11 cases, 7 recognized during life. All showed high nitrogen content of the blood serum, 5 cases having 1.87 gram and 1.95 gram per liter, 6 between 2.3 grams, 3 over 3 grams. In 4 cases, cultures from the pericardium showed no growth, 2 cases showed *Bacillus coli* which did not, however, agglutinate the patients' serum collected ante mortem, 1 showed streptococcus, and 4 pneumococcus, 2 of which had concomitant pneumonia. From these and similar observations, Widal and Weill believe that pericarditis in Bright's disease is a manifestation of marked nitrogen retention, of equal importance on this account as for its localization.

**The Relative Value of Immediate and Delayed Laparotomy in Pneumococcal Peritonitis.**—To attempt to estimate the effect of immediate laparotomy in pneumococcal peritonitis, H. C. CAMERON (*Proc. Roy. Soc. Med.*, 1912, v, Clinical section, 123) has analyzed the cases admitted to Guy's Hospital during the last nine years. Of the 19 female cases, 15 occurred between the ages of five to fifteen

years; of the 7 male, all were aged under twenty-two years. The disease is an acute peritonitis due to a pneumococcus septicemia, characterized in addition by the great and rapid exudation of fluid into the peritoneal cavity. The diagnosis is suggested by the patient's age and sex; by an onset with rigors, convulsions, or herpes labialis; by the early appearance of delirium or pronounced diarrhea; by the simultaneous presence of pleurisy, pericarditis, or pneumonia. The course is a two or three weeks' fever, suggesting typhoid, but with more intense abdominal symptoms. At the end may be left a residual collection of pus, often sub-diaphragmatic, sometimes more diffuse, forming with greater rapidity than in tuberculous peritonitis. In those who pass successfully through the septicemia, recovery may take place. A minority of cases die as a result of failure of drainage of residual pus collections. Cameron believes that there is no evidence that laparotomy at the onset increases the chances of recovery from the septicemia, or helps to cut short the process in the peritoneal cavity. So it is wiser to delay operation until the disease has become localized in the peritoneum, just as is done in dealing with the empyema following pneumonia.

---

**The Relation of Chorea to Rheumatism; An Analysis of 300 Cases.**—M. S. FRASER (*Practitioner*, 1912, lxxxviii, 461). The object of this paper is to discuss the clinical evidence in regard to the relation of chorea to rheumatism. From his analysis, Fraser finds that 53 per cent. of his series showed definite evidence of rheumatism either previously to or concurrent with the attack of chorea; 72 per cent. had either a personal or strong family history of rheumatism. In a large number there was a history of nervous diseases in other members of the family. In comparing the age incidence, Fraser, agreeing with Guthrie's figures, found a marked increase in chorea between six to twelve years, and in acute rheumatism between seven to twelve years. The seasonal incidence, agreeing with Gabbet, showed the maximum of chorea one month later than rheumatism. According to Batten, 25 per cent. of 115 chorea patients treated at the time, without signs of rheumatism, developed it within six years. In regard to the relation of previous disease, Fraser's figures showed that measles and whooping cough had no connection with the onset of chorea. Neither scarlet fever nor diphtheria seemed of any appreciable importance. Hence, Fraser believes that the majority of choreas are closely associated with rheumatism, and that possibly all cases of true chorea are rheumatic in origin, with chorea a cerebral manifestation.

---

**The Causes of Death in Tabes.**—CHARLES W. BURR (*Jour. Nerv. and Ment. Dis.*, 1912, xxxix, 145) finds that persons suffering from chronic degenerative diseases of the spinal cord do not, as a rule, die from them, but from some general affection attacking other organs. This is typically true of tabes, though sometimes the disease may be indirectly the cause of death. The observation of accompanying lesions is of practical therapeutic importance, since treating them may lead to prolongation of a life bearable for the patients. To emphasize the necessity of thorough diagnosis, Burr gives the protocols of 34 cases. General arteriosclerosis is so common as to be regarded as part of the



morbid anatomy of tabes. Chronic myocarditis, valvular heart disease, and chronic nephritis were noted most frequently. Aneurysm was found in 3 cases, not causing death; 6 died from pulmonary tuberculosis; 5 from croupous pneumonia; 2 from septicemia from bedsores. In conclusion, Burr considers his figures are of no value save to show that death in tabes may come from some complication early, or may be delayed for many years. So the life of a tabetic is not definitely limited. It may be long or short, the disease not progressing evenly.

**The Value of the Antigen Reaction of Debré and Paraf for Rapid Diagnosis of Urinary Tuberculosis.**—M. CHEVASSU (*Presse Méd.*, February 28, 1912, xvii, 173). Debré and Paraf have used for diagnosis of renal tuberculosis a modification of the Bordet-Gengou reaction. In a suspected case they have used for antigen the patient's urine, for antibody, known tuberculosis serum, and have tested the deviation of complement against a hemolytic system of sheeps' corpuscles and anti-sheep serum. Chevassu reports with this method a series of 29 cases controlled by autopsy or operation, 15 cases controlled by guinea-pig inoculation, and 36 cases not controlled save by clinical observation. Little stress is laid on the last. Chevassu finds that this reaction gives exact results in nine-tenths of the cases. In none was a negative reaction obtained with a positive control. On the whole, Chevassu concludes that this method is of great value for the rapid positive diagnosis of renal tuberculosis, but of greater value negatively. For the failure to find organisms in urine has never been significant, and a negative inoculation is far less convincing than a positive.

**On the Lesions Produced in the Appendix by Oxyuris Vermicularis and Trichocephalus Trichiura.**—From reviewing the literature, R. L. CECIL and K. BULKLEY (*Jour. Exper. Med.*, March, 1912, xv, 225) find that of parasites observed in the appendix the most common are oxyuris and trichocephalus, but that there has been slight effort to determine whether their presence is fortuitous, a predisposing factor for disease, or the existing cause of it. They have therefore studied 148 unselected appendices of children between the ages of two and fifteen years to determine the frequency of incidence of parasites, the percentage of cases in which specific lesions could be demonstrated, and the character of each. Oxyuris was found more commonly. The series of controls was so small that no definite conclusions could be drawn, but Cecil and Bulkley believe that as 7 per cent. of healthy children, according to Schloss, have oxyuris, such a percentage or less would probably represent its incidence in the normal appendix of children. In disease, the pathological picture seemed characteristic. Grossly the organ is moderately swollen and rigid, the lumen filled with blood and mucus. The mucosa is swollen and more velvety than normal. In most cases, in the neighborhood of the parasite are usually purpuric spots or small hemorrhagic ulcers. There is no suppuration, gangrene, or perforation. Microscopically, where the oxyuris has invaded the mucosa, but with little destruction of tissue, there is extensive extravasation of blood through the ruptured epithelium into the lumen, but without inflammatory reaction. In more marked cases

there is necrosis of the mucosa, with formation of ulcers characterized by hemorrhagic bases, undermined edges, and no reaction save with secondary infection. The process may heal with encapsulation of the worm. Hence they conclude that oxyuris in a diseased appendix may produce characteristic lesions, and in most cases is the exciting cause of the pathological changes found. The trichocephalus cases were few. These parasites show a tendency to burrow along beneath the columnar epithelium in contrast to the oxyuris, which penetrates more deeply. Otherwise the picture is not distinctive.

**The Avoidance of Anaphylactic Phenomena on the Injection of Immune Serum.**—E. FRIEDBERGER and S. MITA (*Deut. med. Woch.*, 1912, xxxviii, 204) review the various methods which have been proposed for the prevention of serum disease, of which Besredka's is the best. An experiment of Bordet's suggested to Friedberger and Mita a new procedure which they have tested experimentally on guinea-pigs. The animals were first sensitized to horse serum and then the fatal dose of serum when injected intravenously was determined. The remaining animals were given varying amounts of serum, *i. e.*, one or more times the fatal dose, all injections being intravenous. It was found that when the serum was injected very slowly eighteen to sixty minutes), as much as ten times the fatal dose could be administered safely. Friedberger and Mita believe their results warrant trial of their method by clinicians when it becomes necessary to re-inject an individual with the same kind of serum or in cases where hypersusceptibility is suspected.

**Urobilin and Bilirubin in Human Blood Serum.**—O. ROTH and E. HERZFELD (*Deut. med. Woch.*, 1911, xxxvii, 2129) have examined the sera of more than 80 patients, many with marked urobilinuria, for the presence of urobilin and urobilinogen, using the zinc acetate and Ehrlich's aldehyde reactions, respectively. All results have been negative. On adding urobilin to serum, it may be readily detected in this manner. But when a few red blood corpuscles are present in the serum the test for urobilin quickly disappears if the mixture be shaken a few minutes, suggesting that the urobilin has been oxidized. Next, they treated alcoholic solutions of urobilin with nascent oxygen and with carbon dioxide and found that oxygen causes a disappearance of the urobilin, whereas carbon dioxide is without effect. They now added urobilin to two portions of defibrinated blood; the one was shaken in the air and urobilin quickly disappeared, while the other, previously saturated with carbon dioxide, showed no loss in urobilin. If oxidation explains the absence of the pigment in the blood serum, it should be possible, by reduction, to demonstrate urobilin in the serum of patients with marked urobilinuria. By the addition of zinc to such serum, urobilin was demonstrable, but the results were not constant, as in the oxidation experiments. A single experiment with a piece of fresh rabbit's kidney in place of the zinc gave a positive result, but there has been no opportunity to repeat this. The reported presence of urobilin in the serum of fatal cases of pneumonia they attribute to possible lowering of oxidation in the body. Practically all patients gave positive, though often weak, reactions for bilirubin in the serum.

**On the Determination of Urea in the Urine.**—O. FOLIN (*Jour. Biol. Chem.*, 1912, xi, 507) describes a new method for determination of urea in the urine. "The urine is diluted so that 1 c.c. contains 0.75 to 1.5 mgms. of urea nitrogen. Dilutions of 1 in 20, 1 in 10, or rarely 1 in 5 are usually adequate for this purpose. One cubic centimeter of the diluted urine is then transferred by means of an Ostwald pipette to a large Jena test tube (2000 mm. by 20 mm.) previously charged with 7 grams of dry potassium acetate (*free from lumps*, 1 c.c. of 50 per cent. acetic acid, a small sand pebble, or better, a little powdered zinc (not zinc dust) to prevent bumping during the boiling, and a temperature indicator. The test tube is then closed by means of a rubber stopper carrying an empty narrow 'calcium chloride' tube (without bulb) as a condenser. (size of calcium chloride tube, 25 cm. by 1.5 cm.). The test tube and condenser are then suspended by a curette clamp so that it can be easily raised or lowered with reference to the small flame of the micro-burner. As soon as the acetate is dissolved and the mixture begins to boil, which usually occurs in about two minutes, the indicator begins to melt, showing that the desired temperature (153° to 160° C.) has been reached. The boiling is continued in a gentle, even manner for ten minutes, at the end of which time the decomposition of the urea is already completed. The apparatus is removed from the flame and the contents are diluted by the addition of 5 c.c. of water. The water is added by means of a pipette through the calcium chloride tube so as to rinse the sides of the tube and the bottom of the rubber stopper from traces of ammonium acetate which may be there. Not more than 5 c.c. of water should be used for this purpose. An excess of alkali, 2 c.c. of saturated sodium hydrate or potassium carbonate solution, is added and the liberated ammonia is driven off by means of a strong air current into a 100 c.c. measuring flask containing about 35 c.c. of water and about 2 c.c. of  $\frac{N}{10}$  acid. The time required for this will, of course, depend on the strength of the air current. (In Folin's laboratory ten minutes suffice.) The ammonia thus set free is determined colorimetrically against 1 mgm. of nitrogen in the form of ammonium sulphate (see total nitrogen method)". For further details, consult the original communication.

**Painting the Peritoneum with Tincture of Iodine in Tuberculous Peritonitis.**—A. HOFMANN (*Münch. med. Woch.*, 1912, lix, 531) reports very good results in the treatment of four cases of tuberculous peritonitis—both dry and exudative. The treatment consisted in opening the peritoneal cavity evacuating fluid, if present, and painting the peritoneal surfaces of the gut and the abdominal wall with 10 per cent. tincture of iodine. Soon after the operation, the peritoneal cavity filled with exudate, but there were practically no fever and no subjective symptoms. In the course of two weeks, the exudate disappeared. The duration of treatment was about four weeks. Subsequent examination of all four cases seemed to show that they were cured. The beneficial effects of this treatment are evident at a much earlier date than with simple laparotomy. The value of the tincture of iodine is due partly to the intense hyperemia of the peritoneum, which is produced.

## SURGERY

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**Evidence of Occult Blood in the Stools and Stomach Contents and its Relation to the Diagnosis of Surgical Conditions of the Stomach, Especially for the Early Diagnosis of Gastric Carcinoma.**—ZOEPPRITZ (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxiv, 538) says that the guaiac test, properly applied, is sufficiently exact and dependable for clinical use. In stomach diseases the opportunities for demonstrating the presence of occult blood are especially favorable because not only the stools, but the stomach contents can be examined and the results in both can be compared with each other. Blood not coming from the stomach may be found in the vomit, but it is of slight importance when the proper precautions are taken against sources of error. The regular finding of occult blood is the most constant and dependable non-specific symptom of gastric carcinoma and is an early symptom of the same. It is already present when the patient seeks aid of the physician. Negative blood findings in the stool speak almost absolutely against gastric carcinoma. Regular findings of occult blood in the stools and stomach contents, in the presence of subjective stomach symptoms, speak for a probable carcinoma and indicate an exploratory laparotomy. For a recurrence of carcinoma of the stomach, the recurrence of occult blood findings is the first alarming symptom. In the very rare cases in which the gastric carcinoma does not respond to the guaiac test this is due not to the absence of blood but probably to the presence of substances which destroy the blood pigment.

---

**A Contribution on the Transplantation of Bone.**—BASCHKIRZEW and PETROW (*Deut. Zeit. f. Chir.*, 1912, cxiii, 490) found by experimentation on rabbits that in free bone transplantation most of the bone pieces soon died. Some of them, which were more viable than others or met with especially favorable conditions for nourishment, remained alive a long time but they finally died of exhaustion. For the regeneration of bone transplanted in the muscle layers, the retention of the periosteum and medulla is not absolutely necessary. Resorption will proceed in a large piece of bone deprived of its periosteum and transplanted between the muscle layers, and it may heal in and be replaced by new bone tissue. The regeneration is much better in an autoplasmic than in a homoplastic transplantation. The destructive process is much

less active but the bone substitution is more active and more complete. The chief source of regeneration in a piece of bone transplanted between the muscle layers, is in the young connective tissue elements which grow around the bone, pressing into the medulla, vessel spaces, and small canals and which undergo metaplasia into osteoblasts and bone cells. The covering of periosteum and endosteum undergoes partial necrosis. The remaining portions may be capable of regenerating new bone, but the permanence of this production is questionable and its differentiation from that produced by the new connective tissue is often impossible. One should, therefore, assume that a covering of periosteum on the transplanted bone is an advantage. The role of the periosteal covering has not yet been explained, although it is evidently a useful one. The quicker adhesion of the transplanted bone to the surrounding tissues, the retardation of the all too rapid absorption, the early impulse toward new bone formation, are so many favorable conditions associated with the periosteal covering. A transplanted piece of bone which has healed in and has died, will not lead to bone formation after a long time. The fundamental point supported by free osteoplasty is that of the transplantation of living bone. The reaction of the surrounding tissue upon the transplanted bone varies greatly according to whether the bone is from the same patient or not, is covered with or deprived of periosteum, or is living or dead.

---

**Low Position of the Transverse Colon.**—SMOLER (*Zentralbl. f. Chir.* 1912, xxxix, 417) says that there are cases in which the ptosis of one organ, although accompanied by a general enteroptosis, stands out prominently in the clinical picture. In those the replacement and fixation of this organ in its normal place, is the only treatment which can free the patient permanently of his troubles. This applies to the kidney, liver, and stomach, and a proper choice of cases will usually be followed by favorable results. Much more rarely will a ptosis of an individual loop of intestine be responsible for the clinical picture. Smoler reports such a case. A woman, aged thirty-five years, had suffered for years from pain in the abdomen which was especially frequent at night and disturbed her sleep. The patient often had the sensation of a distended transverse coil of intestine. The x-rays showed a high grade of ptosis of the transverse colon, which reached almost as low as the symphysis pubis. The stomach was slightly dilated. Through a median incision above the umbilicus, the transverse colon could not be seen until it was drawn up. A reef was taken in the transverse gastrocolic omentum and on one side was fixed to the round ligament by suture, on the other side to the anterior surface of the stomach. The after-course was without incident. The x-rays showed the transverse colon in about its physiological position. The bowel movements which before the operation required laxatives, were afterward spontaneous, and there was no disturbance of sleep. The patient now enjoys complete health.

---

**Paralysis after the Use of Esmarch's Tourniquet.**—KAUSCH (*Zentralbl. f. Chir.*, 1912, xxxix, 499) says that because of the danger of consecutive paralyses, some surgeons will not employ Esmarch's tourniquet especially in the arm. Kausch believes that the paralysis can be avoided by a proper technique. He makes much use of local

anemia, but avoids it in arteriosclerosis and diabetic gangrene. He has had only 1 case which developed paralysis. In this one the tourniquet was applied much too tightly and there remained for some time after its removal a deep furrow. The circulation returned quickly in the usual manner, but at the site of the furrow there was a swelling and very painful infiltration, which disappeared only after about four weeks. The three nerves were totally paralyzed. Three months after the operation, active motion was first observed in the fingers, and six months after the operation all the muscles could be moved voluntarily, but were still weaker than on the opposite side. Not enough attention is given by the surgeon to the application of the tourniquet, which is usually left to one of the younger assistants. Kausch employs a broad bandage, 10 to 15 cm. wide. In applying it the middle is drawn tightest, the edges less. In aseptic cases the limb is made bloodless from the periphery upward, the bandage being applied weakly at first and gradually more strongly. Local foci of infection are passed over. In a case of diffuse infection, the limb is not rendered bloodless from the periphery upward, but is held vertically for ten minutes. The bandage is then applied quickly, immediately constricting all the vessels, not vein first and then arteries, because this would cause a venous hyperemia.

---

**Hematuria of Nephritis and Renal Papillitis from a Surgical Standpoint: A Study of 73 Cases.**—BARRINGER (*Amer. Jour. Urol.*, 1912, viii, 229) says that in these 73 cases there was a large proportion of cases of mild toxic nephritis, probably unilateral, giving no classical symptoms of nephritis, and giving rise to or accompanied by unilateral hematuria, the hematuria being out of all proportion to the nephritis present. There was a small proportion of cases of infectious nephritis, probably unilateral, giving rise to unilateral hematuria. There was a small percentage of cases of typical toxic nephritis, giving rise to the symptoms and urinary findings of nephritis, and giving rise to hematuria, probably, as a rule, bilateral. There was an indefinite number of cases of pelvic conditions variously named varicose veins of the papilla, pyelitis cystica, metaplasia of the renal pelvis, etc., giving rise to unilateral hematuria. In a large proportion of cases these pathological conditions of the kidney pelvis or papilla are caused or accompanied by a nephritis, toxic or infectious. Hemorrhagic nephritis is most frequently confused with kidney stone, tuberculosis, and neoplasm. The differential diagnosis between hemorrhagic nephritis and neoplasm is alone considered. In the former the age is from twenty to fifty years, in the latter from forty to seventy years. In the former, tumor is absent in probably 80 per cent. of the cases, in the latter is present in 60 to 80 per cent. In the former the hematuria is constant, in the latter it is present in most cases. In the former the duration of the hematuria is from days to thirty years, in the latter if it extends into years all neoplasms but hypernephromas may be excluded. In the former the hematuria may persist for years with no tumor, in connection with the latter there is a small percentage of cases of hypernephroma where hematuria has existed for some years and in which no tumor is present. This is not so in other neoplasms. In the former the functional capacity is generally normal, in the latter generally decreased. In the former the pain or kidney tenderness is often present,

which is also true of the latter. In the former varicocele is absent, in the latter it is present in one-fourth of the cases. If there is any doubt about the symptoms, if the diseased kidney be enlarged or if the patient be a poor subject for palpation; if the function of the diseased kidney be one-half or less than that of its fellow, or if the bleeding has endured less than four years, an exploratory laparotomy for diagnosis should be done. In a majority of cases operation was primarily performed for diagnosis and not for cure of the hematuria. There is no reason for nephrotomy either to arrest hemorrhage or for diagnosis. Nephrectomy is contraindicated unless there is danger of death from hemorrhage. If the diagnosis can be made there is no indication for operative interference unless other means to stop the hematuria fail. These nonoperative means are: rest in bed; internal administration of turpentine; injection of adrenalin into the renal pelvis. Of operative methods to arrest the hemorrhage either decapsulation or pyelotomy or both seem more adequate than nephrotomy or papillotomy.

**The Technique of Paravertebral Nerve Anesthesia.**—FINSTERER (*Zentralbl. f. Chir.*, 1912, xxxix, 601) has employed this method of anesthesia in 6 laparotomies. In two colostomies, the results were negative, it being necessary to infiltrate also the deep tissues in order to complete the operation without narcosis. In the remaining 4 cases complete anesthesia was obtained. The technique is as follows: The spine of the first lumbar vertebra is first determined by palpation, when 3 to 3½ cm. from the median line, after anesthetizing the skin, an injection needle marked in centimeters is passed vertically to a depth of 4 to 5 cm. according to the thickness of the tissue, until the transverse process is struck. The needle is then made to feel for the upper border of the process, when by carrying the syringe outward and downward the needle is made to pass inward and upward and is pushed forward ½ to 1 cm. Five cm. of a 1 per cent. solution of novokain are then injected in a fan-shaped area. One must be careful not to push the needle too deeply when the anesthetizing fluid would be injected beyond the ganglion and be useless. The points for injection of the 1st, 2d or 3d lumbar nerves, will be at intervals of 3½ to 4 cm. according to the size of the individual. The transverse process is to be employed as the guide as in the first injection. Of the 4 successful cases, one was a woman, aged eighty-one years, operated on for a diffuse peritonitis. In the second the patient was a cachectic man, aged forty-seven years, operated on for a chronic ileus from an inoperable carcinoma for which an ileocolostomy was done. The third case was that of a man, aged fifty-three years, with a tuberculosis of both lungs, in whom an artificial anus was made. The fourth case was that of a man, aged nineteen years, who was operated on for an acute recurring appendicitis. The method is not advised as the routine procedure in operations for appendicitis or colostomy. It should be employed when severe diseases of the lungs make a short ether narcosis dangerous and especially for the extirpation of tumors of the cecum and sigmoid flexure and for ileocolostomy, in patients who are much depressed.

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

**Calcium Salts in the Treatment of Asthma.**—KAYSER (*Therap. Monatsheft.*, 1912, xxvi, 165) has treated 13 cases of asthma and similar conditions prophylactically by calcium chloride. He gave the calcium chloride in the form of a solution containing 20 gm. of calcium chloride, 40 c.c. simple syrup, and distilled water up to 400 c.c. The patient was given a tablespoonful of this solution in milk every two hours for a period of eight days. The patients all noticed a distinct improvement; their breathing and expectoration became much easier and their sleep was not disturbed by attacks of dyspnea. In all but 2 cases no attacks of dyspnea and cough occurred after three days of treatment. In some of the cases the freedom from attacks has been permanent. Kayser explains the action of calcium chloride in asthma by its sedative action upon the nervous system and he cites its beneficial effect in other nervous affections.

**Normal Human Blood Serum Injections in Melena Neonatorum and Other Conditions.**—WELCH (*Therap. Gazette*, 1912, xxxvi, 81), drawing his conclusions from an experience with 32 cases of hemorrhagic conditions, treated by normal human blood serum, is convinced that this agent is specific in its action in controlling the bleeding. He gives the details of some of the cases he has treated and refers to a previous communication on the same subject. He does not believe that injections of defibrinated blood have any advantage over injections of serum. He says that experiments made by Ehrlich have demonstrated that the red blood cells injected into the same species call forth a hemolytic body for their digestion and removal, which he calls isolysin. In the production of the isolysins a certain amount of cellular energy is consumed which is just so much extra tax on the individual capacity for general resistance. The serum is so easily obtained that Welch can see no reason for using whole blood, especially in babies, thereby possibly reducing the strength of the child, already at the lowest ebb. Transfusion of blood is of great value, but is accompanied by certain dangers. Hemolysis, thrombosis, and embolism, all or any of which may lead to the death of the patient, are to be feared. The practical disadvantages of transfusion are, first, the difficulty of the operation which is not so simple as many suppose; secondly, it is frequently necessary to repeat the transfusion and this is a great disadvantage, while on the other hand normal blood serum can be repeated frequently and used indefinitely. However, for certain cases of very marked depletion from prolonged hemorrhage—the only measure offering any hope is transfusion.



**Camphor and Pneumococci.**—SEIBERT (*Med. Record*, 1912, lxxxi, 750) reports his results with injections of camphorated oil in pneumococcic pneumonia. He says that the injections invariably reduce the toxemia until practically normal conditions were reached three or four days after the first injections, while the alveolar exudate remained, to be absorbed later on. This phenomenon and the absence of a crisis were noticed in every case. He gave 12 c.c. of a 20 per cent. camphorated oil every twelve hours to adults and 6 c.c. to children, irrespective of the intensity of the toxemia and the extent of the local process. In a subsequent series of patients the results were apparently not so favorable. In 2 cases of severe pleural pneumonia the camphor reduced the general toxemia markedly but did not prevent a subsequent empyema. However, both these patients recovered after an operation. Two other patients had a sudden rise of temperature on the second and third days of the treatment but the camphor injections were continued and both patients recovered. This exacerbation proved to be due to pneumococcic nephritis and promptly subsided under treatment by hexamethylenamin. Of 37 cases of pneumonia so treated only one resulted fatally. This patient was a man, aged sixty-eight years, weighing 200 pounds, with a fatty heart, who had a double pneumonia with marked toxemia. The camphor injections had a good effect upon the sensorium, the temperature and the respiration, but his heart gradually failed and he died on the sixth day. Seibert also relates animal experiments with camphorated oil injections in 20 animals simultaneously inoculated with fatal doses of pneumococci. Death was prevented in 9 of the animals and retarded from two to five days in 8 more. He believes that camphor injections in human and animal pneumococcic infections materially assist in overcoming the toxemia. He found that injections of 10 c.c. of a 30 per cent. camphorated oil (equal to 36 grains of pure camphor) to 100 pounds of human body weight every eight to twelve hours are entirely harmless.

---

**The Treatment of Melena Neonatorum by Human Blood Serum.**—NICHOLSON (*Therap. Gazette*, 1912, xxxvi, 77) reports a case of melena neonatorum treated by injections of normal human blood serum with complete recovery. Nicholson believes that the subcutaneous or intramuscular injections have a distinct advantage over actual transfusions for two reasons: (1) That the latter requires special skill for its performance, it being a delicate operation even in the adult and requiring special appliances; and (2) the difficulty in obtaining suitable donors. He believes that the injection of blood serum is a very practical measure and so very useful in combating emergencies.

---

**Untoward Results from Transfusion of Blood in Pernicious Anemia.**—BENNECKE (*Münch. med. Woch.*, 1912, lix, 571) refers in this article to the lack of benefit resulting from intravenous injections of defibrinated blood in the treatment of pernicious anemia. The article is apparently a criticism of a number of observers who have recommended the intramuscular or subcutaneous injections of defibrinated blood for the treatment of pernicious anemia. The transfusions were used as measures of last resort in the cases reported by Bennecke usually in the terminal stages of the disease and therefore the test of even the intra-

venous injections of defibrinated blood was not entirely fair. Bennecke treated 5 cases and the treatment was followed by an increase in the hemoglobin and red blood cells in only one case. This improvement might have been explained, according to Bennecke, by a spontaneous remission of the disease. Bennecke believes that the injections are not entirely without danger and he thinks that death was hastened by them in one case at least.

---

**Vaccine Therapy in Rheumatoid Arthritis.**—HORDER (*Lancet*, 1912, clxxxii, 1053) says that in every case of rheumatoid arthritis careful investigation should be made to determine any possible focus of local infection. The mouth should be carefully investigated, also the fauces, the nose, the naso-pharynx, nasal sinuses, the respiratory tract, the small and large intestine, the urinary tract, and the uterus. Any lesion in one or more of these situations should be investigated bacteriologically. If any infective focus is found, there must be evidence of a causal connection between the predominating organism and the arthritis. Before beginning vaccine treatment the focus of infection must be treated locally. It must be drained or subjected to the necessary surgical measures for its eradication. Horder says that, in actual practice, the microorganism most often found as the infective element of the disease is a type of streptococcus, not streptococcus pyogenes; but streptococcus salivarius or streptococcus fecalis, streptococci of relatively low virulence, not tending to suppuration and traceable, as the name suggests, to the mouth or intestine. Other microorganisms are much less common; the gonococcus, pneumococcus and the colon bacillus, have also been found by competent observers. Possibly Staphylococcus aureus or albus, influenza bacillus, and certain bacilli related to the diphtheria bacillus may be included in this list of bacteria. The initial dose of vaccines should be small and the dosage should be very gradually increased. Horder recommends the vaccine treatment especially for chronic cases and it should be continued for at least three months before definite conclusions can be drawn as to its results. He says that of course organic changes in the joints cannot be influenced by the treatment, but that many cases seem to change from an active to a quiescent stage and a few appear to be entirely arrested. The vaccine treatment should be discontinued upon the occurrence of increase in pain, stiffness or swelling of the joints, loss of weight, or nervous disturbances.

---

**Subcutaneous Injection of Small Quantities of Human Blood in Spontaneous Hemorrhage of Newborn.**—MEYERS (*Arch. of Pediatrics*, 1912, xxix, 197) relates the history of a child who, when thirty-two hours old, had repeated stools composed entirely of tarry blood clots. The hemorrhage from the bowels was accompanied by the vomiting of considerable quantities of clotted blood. At the end of twenty-four hours of this repeated bleeding the child's condition seemed practically hopeless. The weight had fallen to four pounds and eight ounces and the skin and mucous membranes were almost bloodless. Meyers injected into the subcutaneous tissues of the baby's buttock 3 c.c. of blood withdrawn from a vein of the mother's arm. The injection was made quickly so that the blood could not coagulate. A slight hemor-

rhage from the bowels occurred two and one-half hours after this injection. A second injection of 5 c.c. of maternal blood was given about five hours later. After this injection the bleeding was not repeated and the child's nutrition rapidly improved. The blood injected was quickly absorbed and a few hours afterward the site of the injection could be recognized only by the needle puncture. The doses used by Meyers were much smaller than those reported in cases treated by Schloss and Commiskey who reported 6 recoveries in 7 cases treated with injections of from 10 c.c. to 20 c.c. of fresh blood, a varying number of injections being used for each case. The fatal case was in an infant who had suffered from multiple hemorrhages for eight days and was in a moribund condition when treatment was begun. This patient died three and a half hours after admission to the hospital, having received only a single injection of 10 c.c. of blood.

---

**The Results of Anti-typhoid Vaccination in the Army in 1911, and its Suitability for Use in Civil Communities.**—RUSSELL (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1331) gives a brief review of antityphoid vaccination from its introduction in 1896 to the present time. He believes that the lack of uniform success with the earlier inoculations was due to faulty technique in the preparation of the vaccine. The vaccine used in the United States Army inoculations is prepared by growing an avirulent strain of typhoid bacilli on agar for twenty-four hours. The resultant growth is washed off in normal saline solution, standardized by counting the bacilli, killed by heating to 55° C. for one hour and then 0.25 per cent. of tricesol is added as a matter of safety. Preliminary experiments with the vaccine prepared in this manner showed that it produced a high degree of immunity without, at the same time, causing severe general or local reactions. The vaccine is injected into the subcutaneous tissue (not into the muscles or into the skin) of the arm, at the level of the insertion of the deltoid muscle, the necessary skin sterilization having been accomplished by tincture of iodine. Three injections are given at ten day intervals—the first contains 500,000,000 bacteria, the second and third 1,000,000,000 each. As a rule, there is a local reaction consisting of a red and tender area about the size of the palm of the hand, which usually subsides within forty-eight hours. The general reaction, when present, shows itself by malaise, headache, fever, occasional chills, quite rarely by nausea, vomiting or diarrhea, and in exceptional instances by transient albuminuria. General reactions rarely appear in children and in young people and a severe reaction occurs in only one to three persons per thousand. Russell gives some very striking tables comparing the incidence of typhoid fever in the troops at Jacksonville in 1898 with those mobilized in the recent army maneuvers at San Antonio, Texas. The two divisions were encamped under nearly the same conditions although camp sanitation was probably much better in the case of the maneuver division. Of 10,759 in the Jacksonville camp there were 1,729 undoubted cases of typhoid and 964 additional cases in which the diagnosis of typhoid was probable. In all there were 248 deaths due to typhoid fever. Of 12,801 in the maneuver division, only one mild case of typhoid fever developed. Russell attributes this striking difference mainly to the fact that the men of the maneuver division had received protective inoculations of

the antityphoid vaccine. During the period of encampment of the maneuver division there were 49 cases of typhoid with 19 deaths. Among the civil population of San Antonio, and in Galveston 192 cases were reported during the same period. The men of the maneuver division frequently visited the cities of Galveston and San Antonio and thus there was frequent chance of infection. Russell believes that antityphoid vaccination is applicable in civil practice to a great extent particularly in epidemics and cites the experience learned from the Toerington, Conn., epidemic. His conclusions are as follows: (1) Antityphoid vaccination in healthy persons is a harmless procedure. (2) It confers almost absolute immunity against infection. (3) It is the principal cause of the immunity of our troops against typhoid in the recent Texas maneuvers. (4) The duration of the immunity is not yet determined, but is assuredly two and one-half years, and probably longer. (5) Only in exceptional instances does its administration cause an appreciable degree of personal discomfort. (6) It apparently protects against the chronic bacillus carrier and is, at present, the only known means by which a person can be protected against typhoid under all conditions. (7) All persons whose professions or duty involves contact with the sick should be immunized. (8) The general vaccination of an entire community is feasible and could be done without interfering with general sanitary improvements, and should be urged wherever the typhoid rate is high.

**Tincture of Digitalis—Its Potency and Keeping Properties.**—GOODALL (*British Med. Jour.*, 1912, 2677, 887) has examined a number of samples of tincture of digitalis during a period of three years with special reference to their strength and stability. He found that nearly 50 per cent. of samples of digitalis made by manufacturing chemists of repute showed a departure from the average standard of potency. The limits of this variation were from 275 per cent. overstrength to 40 per cent. understrength. In other words the effect of a dose of 10 minims might be that of  $37\frac{1}{2}$  minims or of 6 minims. Tincture of digitalis probably retains its full activity for one year, but after that period deterioration of its potency to an important extent is likely to take place.

## PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,  
OF PHILADELPHIA.

**The Treatment of Chorea Minor.**—J. GROBER (*Deutsch. med. Woch.*, 1912, xxxviii, 833) places chorea minor among the acute infectious diseases, and notes the close relationship of this disease to acute articular rheumatism. The portal of entry for the specific cause is presumably the nasopharynx and tonsil, as is the case in epidemic meningitis and

anterior poliomyelitis. This indicates the importance of insisting on thorough and regular cleansing of the mouth and pharynx of the patient with antiseptic gargles and mouth washes. In chorea minor the symptoms of an acute infection are limited to the first few days in the form of moderate fever, and occasional sore throat, the fever itself needing little or no treatment. The advent of acute articular symptoms or cardiac involvement calls for special treatment. In associated articular conditions Grober has found no influence on the course of the disease from the use of salicylates or 'aspirin'. On the contrary, these drugs in children often cause physical and mental discomfort. Psychic treatment is of the utmost importance. The absence of all exciting influences, absolute rest, of both body and mind, and isolation in severe cases, are essential. The diet should be soft or liquid, given frequently in small quantities. The knowledge and dexterity of the nurse are important in feeding the severe cases and in protecting their bodies from injury. The crib or bed should be padded on all sides to prevent the patient from injuring himself during violent choreic movements. Immersion for a long period of time in warm baths,  $34^{\circ}$  to  $37^{\circ}$ , three times a day often reduces the choreic movements, induces sleep, and increases the appetite. The effect of the baths is often accentuated by adding brine, salt or carbonic acid. The effects of bathing on the heart must be carefully watched. The treatment of chorea by the galvanic current is useless and the faradic current is harmful. Treatment by massage and gymnastic movements is ill-advised and tends to increase the general irritability. Arsenic has no logical effect on chorea except in influencing the resulting anemia which is due to diminished food intake. Fowler's solution is preferred. In the line of sedatives, Grober prefers the bromides to veronal or chloretone, and in extreme cases uses chloral hydrate. Morphine should not be used except as a last resort. The probability of cardiac involvement makes the use of the last two drugs a serious matter. Some abnormality of the heart occurs in almost every case of chorea. Slight irregularity of pulse or blood flow, albumin and casts in the urine, slight edema of the feet or lower eyelids, peripheral cyanosis and cardiac murmurs can be found and are irregular and inconstant, varying from day to day. In cardiac complication ice caps on the præcordium and immersion in warm baths are of questionable safety. Digitalis and strophanthus are indicated only when loss of compensation is threatened. Good nourishment in convalescence is important and a long period of freedom from school and removal to the country if possible is of the greatest importance in establishing a permanent cure and preventing a relapse.

---

**Duration of the Infectious Period in Scarlet Fever.**—A. BAGINSKY (*Deutsch. med. Woch.*, 1912, xxxviii, 746) submits the results of an investigation into the length of time a scarlet fever case may remain infectious after it has been discharged from hospital as cured. He appends an interesting diagram of 45 "return cases" in which members of the family contracted the disease from children returned as cured. The cases were isolated in hospital for forty-two days, with a few exceptions. Of the 45 cases which carried the infection to their homes, all were apparently perfectly well except 2 suffering from an otitis.

There was no trace of desquamations left in any of the cases. Seven "return cases" spread the infection within three days of their return home. Six cases transmitted infection four days after their return. These cases were all in the hospital for forty-two days, showed no abnormality in any way when discharged and still carried infection back to their families. This shows that the regulation, six weeks isolation is not long enough. The majority of infections occurred between three and four days after the return, although a number occurred up to the seventh day. This substantiates the accepted incubation period. By the process of exclusion Baginsky concludes that in the apparently recovered cases which carry the infection the naso-pharynx is the seat of the infectious substance. Out of 12 cases of scarlet fever occurring suddenly and sporadically on the surgical wards of the hospital 6 of them occurred in cases of burns of the body surface, showing a remarkable relation between scarlet fever infection and superficial or skin burns. Probably the burned child is particularly susceptible and the contagion is present in some near-by, apparently well child. Both Baginsky and Sommerfield look to the streptococcus as one of the chief factors of this contagium of scarlet fever. No one can say exactly how long a case should remain in isolation, but it is clear that the period should be longer than the present regulation of six weeks. Baginsky suggests the establishment of stations or convalescent homes where children can be kept for a time and observed after their discharge from hospital as apparently cured.

---

**Significance of the Facialis Phenomenon in Later Childhood.**  
—H. NEUMANN (*Deutsch. med. Woch.*, 1912, xxxviii, 813) describes the facialis phenomenon as a sudden contraction or spasm of the muscles of the nose, eye, and forehead, supplied by the facial nerve, when a sharp tap is given over a point midway between the zygomatic arch and the corner of the mouth on one side. At times fibrillary twitching around the eye and nose take the place of the combined spasm of the muscles. This phenomenon is of great value in the diagnosis of infantile tetany and in the prevention and treatment of laryngismus stridulus and allied spasms. This phenomenon is even more frequently found during early school-life than during the first years of life. The facialis phenomenon in older children is possibly the evidence of a masked infantile tetany. Not only does this phenomenon indicate a masked tetany through increased motor irritability of peripheral nerves, but it shows a relation to neuropathic conditions and has been found present in 50 per cent. to 80 per cent. in neuropathic children, aged between four and eighteen years. As this age increases the phenomenon appears less marked. Again, the condition may not develop until during adolescence and tetany and isolated facialis phenomena in late adolescence have a particular relation to hereditary neuropathy. The phenomenon is found in a large number of children with abnormal psychic and sensory irritability, as evidenced more or less by over-sensitiveness to sights and sounds, in disturbances of normal sleep, and in terrors of various kinds. The presence of the facialis phenomenon often leads to the discovery of these general symptoms. The strength of the phenomenon, however, does not indicate the grade of the neuropathy. The phenomenon is a valuable objective evidence of the neuropathic constitution.

## OBSTETRICS

---

 UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA

---

**The Cause of Rupture in Tubal Pregnancy.**—KIUTSI (*Archiv f. Gynäk.*, 1911, Band xciv, Heft 2,) gives the results of his extensive study of this question in Veit's clinic in Halle. His paper is fully illustrated. He characterizes such rupture as acute bursting of the capsule of the embryo. Examination of specimens show various changes in the villi, extravasation of blood, engorged veins, infiltration of blood in the connective tissue, and symptoms of engorgement. The cause he finds to be the occlusion of veins in the intervillous spaces by the growth of the villi. The arterials bring the blood into these spaces, but the pressure of the villi prevents its return by the veins. This process gradually produces a thinning in the capsule of the embryo. The edges of the opening are not usually covered by fetal cells. The trophoblast does not extend to the edge of the ruptured tissue. If fetal cells rupture the capsule they must always penetrate the maternal tissue, and in such a case would even attack the peritoneum. A growth of the villi may be described as apoplexy of the villi, as ischemia of the villi, or as a combination of the two. If the tissues are greatly compressed the apoplectic portion is usually on the periphery at the summit of the villus. The fetal erythroblasts often take the form of free nuclei. These specimens also show in the neighborhood of the principal rupture of the capsule, the giving way of intracapsular tissue by congestion, and extravasation of blood in the connective tissue. The inner layers of the capsule undergo retrogressive changes. The hemorrhage which threatens the patient's life occurs when rupture of the tissues opens the small arteries; also when the tissues surrounding these vessels are comparatively thin, and no efficient stoppage of the hemorrhage from pressure develops. The death of the embryo results from the disturbance of circulation in the villi, and is of secondary consequence to the intervillous congestion. In general, the bursting of the pregnant tube results from abnormal growth of villi, dilatation of veins, and intervillous extravasation of blood. Mechanical violence or contraction or torsion of the tube favor this. Undoubtedly previous inflammation predisposes to this accident. Observation shows that the ovum can develop in the tube without the presence of mucous membrane.

---

**The Prevention of the Formation of Striæ of Pregnancy.**—Those patients who object to the formation of the characteristic striæ of pregnancy, and consider them a deformity, may find comfort in BARFURTH'S success in the clinic at Rostock, in preventing this change by massage (*Zentralbl. f. Gynäk.*, 1911, No. 51). Barfurth reports 12 cases in which massage was given by student midwives. Those portions of the abdomen where striæ most often develop were treated by

stroking motions, pressure being gently exercised upon the tissue held between the thumb and finger. The abdominal skin was massaged in circular and radial motions from the umbilicus, and the tissues of the breast were similarly treated. The thighs and hips were massaged in various directions. Oil was used before the massage. In most cases daily massage of fifteen to thirty minutes sufficed, but where the skin was excessively resisting the patient received two treatments daily. Occasionally manipulation was so painful that it was abandoned. The patient improved if the skin became softer and more distensible. In the great majority of cases the treatment was agreeable to the patient.

---

#### Medical Education and the Midwife Problem in the United States.

—WILLIAMS (*Jour. Amer. Med. Assoc.*, January 6, 1912) sent a list of questions to the professors of obstetrics, in 120 medical schools, giving the full four-year course; 43 replied. When these replies are analyzed, they indicate that many professors are inadequately prepared for their duties, and have but little conception of the obligations of a professorship; that a considerable proportion are not competent to cope with all obstetrical emergencies; that nearly all complain that their teaching and hospital equipment are inadequate for the proper training of students; and a large proportion admit that the average practitioner through his lack of preparation for the practice of obstetrics may do his patient as much harm as the much maligned midwife. As regards what is needed to make the equipment of American medical schools competent for obstetrical training, it was found that this department was unusually inferior to others in ward accommodations, intelligent and educated assistants, and especially in broad-minded scientifically trained teachers, and properly equipped laboratories for investigating work. It is not surprising from this fact to find that one-fourth of the entire number of teachers who replied stated that they did not consider the ordinary graduate from their schools competent to practice obstetrics; while others considered the medical graduate as a fairly efficient man midwife. Williams states that in his own experience students are unfit on graduation to practise obstetrics in its broad sense, and are scarcely prepared to handle normal cases. As regards the attendance in labor cases by midwives, it is found that very few practise in Montreal and but a small number in Boston. In the greater number of large American cities they conduct from 40 to 60 per cent. of all labor cases. There is no efficient and satisfactory control of these midwives in any portion of the country. More than one-half of the teachers replying consider that general practitioners lose proportionately as many women from puerperal infection as do midwives. When the question is raised as to how this bad result is obtained, the majority believe that ill-judged and improperly performed operations, in the hands of the general practitioner, cause as many deaths as result from the mistakes of incompetent midwives. When the question of improving these conditions is raised, general improvement in medical education is a fundamental necessity. Obstetric professors must be especially trained for this work, and devote themselves largely to the care of hospital patients, the proper training of assistants and students, and the advancement of knowledge. Medical



faculties and hospitals must recognize that obstetrics is a fundamental branch of medicine, requiring a scientifically trained man as a teacher, with a broad grasp of the subject. The general practitioner must realize that he is competent to conduct only normal cases of labor, and that major obstetrics, as major surgery, should be undertaken only by especially trained men, in control of abundant hospital facilities. Applicants for license to practise should submit a statement certifying that they have seen, delivered, and personally examined, under appropriate clinical conditions, at least ten women. The public must understand that poorly trained doctors are dangerous, that most of the disorders of women result from poor obstetrics, and that poor women, in fairly well-conducted free hospitals usually receive better care than well-to-do women in their own homes; and that competent obstetricians will be forthcoming so soon as the public is willing to recognize them as such. Obstetric charities must be increased by free hospitals and out-patient service for the poor, and proper hospital accommodations for those in moderate circumstances. Visiting obstetric nurses and helpers trained to work under them, can be of service. Midwives should be gradually abolished in large cities and replaced by obstetric charities. The reviewer gladly contributed replies to the questions sent and considers the investigation most timely. He further thinks that a considerable responsibility lies upon teachers of obstetrics in the conception which they give to medical students concerning this branch of medicine. While the fundamental facts of obstetric surgery should be taught to all graduates, it is the duty of the obstetric teacher to warn the entire class that but a small proportion of them will become competent obstetric surgeons. These only should undertake difficult forceps extraction, version, placenta prævia, eclampsia, craniotomy, opening the pubic girdle, Cesarean section, ectopic gestation, separation of the placenta, and ruptured uterus. The majority of a graduating class should early determine whether or not they propose to do surgery, obstetric or other, and unless they find themselves with unusual ability and equipment they should decline obstetric surgery. Normal parturition without complications comes within the scope of the average graduate and practitioner, provided he is not in a position to infect his patient. Medical graduates and general practitioners sometimes allege that obstetrics belong to general practice. By some who cater to the general profession for consultations, obstetrics has been termed the specialty of the general practitioner. If successful general practitioners are asked whether they do obstetric work from choice or from necessity, in my experience they invariably reply that they do it only to keep the medical practice of the family. If they could do so, they would be quite willing to turn all prolonged and complicated cases of parturition over to a competent obstetrician, who in return would not interfere with the medical practice of the family. Unless one is able and equipped to do obstetric work it does not pay, and by the demands upon the time and strength of the obstetrician, it interferes most seriously with general medical work. Furthermore, the physician who must treat the exanthematous diseases of childhood, and the various contagious diseases, is not a safe or suitable person to conduct confinements. Radical improvement in this direction will not become general until the economic side

of the problem is demonstrated. When a man learns that in the long run it will cost him less to have his wife receive proper attention in labor, avoiding serious lacerations, and promptly repairing those which are inevitable, he will be willing to pay a fair price for such service. It is cheaper than a badly conducted confinement at a cheap rate and the expense of a secondary operation by a surgeon or gynecologist later. The saving of infant life through competent obstetric work does not always appeal to those who must struggle to make a living. This is, however, a question of national importance, and in other countries has received the careful attention of governments and philanthropists.

---

## GYNECOLOGY

---

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

---

**Vaginal Hysterectomy Under Local Anesthesia.**—RUGE (*Zentralbl. f. Gynec.*, 1912, xxxvi, 561) believes that, while ordinary infiltration anesthesia has a great field of usefulness in gynecology as in other branches of surgery, that produced by blocking the nerve-trunks at a distance from the field of operation is preferable, since the appearance and consistency of the tissue in which the operation is to be performed is not altered. He has devised the following technique for the performance of complete vaginal hysterectomy, and other major vaginal operations. After disinfecting the vagina the long, thin needle of a "Record" syringe is introduced into the parametrial tissue to one side of the cervix to a depth of 4 to 5 cm., being directed in a somewhat lateral direction, in order to strike the nerve trunks before they have undergone their ultimate subdivisions. If the needle is introduced slowly, most vessels, and any coils of intestine with which it may come in contact, will be pushed aside and not injured. Should a vein be punctured, however, blood will begin to flow out of the needle, which must then be drawn back a little, and advanced in a slightly different direction. When the needle has been satisfactorily introduced the 10 c.c. syringe is attached, and, gradually withdrawing the needle, the solution injected. The process is repeated on the opposite side; then at two points in the anterior and two in the posterior vaginal vault similar injections of 3 to 5 cc. of fluid are made. In the anterior vaginal vault it is necessary to introduce the needle 2 to 3 cm. deep, but in the posterior only just through the mucosa. As injection fluid Ruge uses a 1 per cent. novocain solution, to each 100 c.c. of which 5 drops of a 1 to 1000 adrenalin solution are added. It is sterilized by boiling immediately before use. The amount used is about 40 c.c., but it is practically non-toxic, and much larger amounts could be employed with impunity. The vagina is rendered anesthetic by

swabbing it out with a sponge covered with cycloform powder. To eliminate pain from pulling on the bladder, 5 c.c. of the injection fluid are introduced into it through the catheter. It is necessary to wait twenty to thirty minutes for the anesthesia to become effective, but it then lasts one and a half to two hours. Ruge reports having recently operated in this manner on two patients, neither of whom felt anything during the entire operation, not even the introduction of large gauze pads to hold back the intestines, nor seizing the parietal peritoneum with toothed forceps. No morphine, scopolamine, or other narcotics were given. Ruge considers this method just as satisfactory as lumbar anesthesia, and far less dangerous.

---

**Lymphatics of the Clitoris.**—ROUVIÈRE (*Ann. de Gyn. et d'Obstet.*, 1912, xxxix, 273) has been struck by the fact that at times, following extirpation of the clitoris for carcinoma, recurrence takes place in the small pelvis directly, without involvement of the inguinal or retro-crural glands, an occurrence which should be impossible if the classical description of the anatomy of the lymphatics of this region is correct. He has therefore undertaken some investigations into the lymphatic supply of the clitoris, and has been able to demonstrate by injection methods the occasional occurrence of lymph vessels which establish a direct connection between that organ and the hypogastric glands in the pelvis—a finding similar to that of Küttner with regard to the penis. He was not able to find these direct lymph channels in all cases, this being due, he thinks, rather to an irregularity in their occurrence than to any fault in technique. He considers, however, that the demonstration that they do occur in a certain number of cases explains, in part at least, the extremely unfavorable prognosis that it usually associated with carcinoma about the clitoris, since in such subjects it is almost impossible to excise thoroughly the entire tributary area.

---

**Composition of the Menstrual Fluid.**—The results of careful chemical analyses of the fluid obtained from 10 cases of hematocolpos due to atresia are reported by BELL (*Jour. Obst. and Gyn., Brit. Emp.*, 1912, xxi, 209). Urea was never found; mucin, on the other hand, was always present in large amount, arising from the cervix and vagina. Blood, estimated from the amount of iron present, formed on an average somewhat less than 50 per cent. of the fluid. Fibrinogen and fibrin-ferment were always absent; to this fact is due, Bell believes, the non-coagulability of menstrual fluid, and not to the presence of mucin or of lactic acid, as has frequently been taught. He believes that this lack of fibrinogen and fibrin-ferment in the menstrual fluid is the result of some vital function of the healthy endometrium, which destroys or extracts it, since there is nothing in the uterine or vaginal secretions to destroy the fibrin-ferment, or to prevent clotting of the blood if it were present. This Bell has shown by adding to normal sodium fluoride solution an equal quantity of hematocolpos fluid, together with fibrin-ferment, obtaining a good clot within ten minutes. In all the specimens examined lactic acid was found, although all were sterile but two, in which there were some colon bacilli, probably due to contamination during or after removal. In no case were Döderlein's bacilli found. Bell concludes, therefore, that the acidity of the vagina is not due to

this bacillus, but to the lactic acid, which is formed by the action of some cellular enzyme on the mucin present. The calcium content of the hematocolpos fluid was invariably found to be high, amounting in some cases to six times or more that of normal blood.

**Arsenic as a Factor in Menstruation.**—Some rather interesting, even though as yet not entirely conclusive investigations into the arsenic-storing function of the uterine glands have been carried out by IMCHANITZKY-RIES and J. RIES (*Münch. med. Woch.*, 1912, lix, 1084). These authors have demonstrated, by means of the Marsh and Gutzeit tests, the presence of small quantities of arsenic in the endometrium during menstruation. In the post-menstrual stage arsenic is entirely lacking, to reappear later in the interval, being present in the largest amount just before the onset of menstruation. In the endometrium of a woman, aged sixty-five years, they were unable to find any traces of arsenic. The theory of the investigators is that arsenic, a considerable quantity of which is taken in with the daily food, is stored up in the uterine glands, and is given off in the mucoid secretion which is eliminated by them during the pre-menstrual stage, but which remains blocked up in the tortuous glands until it is discharged during menstruation. That menstrual fluid does actually contain arsenic has been demonstrated by Gautier, who found that about 0.15 mg. is given off in this way on an average at each menstrual period. It has been frequently demonstrated that arsenic given therapeutically to men can be recovered in the urine; in women, however, this is not the case, a further confirmation, the authors believe, of their theory that it is stored in the uterine glands. They have found that a much larger quantity of arsenic is always present in the tissues of fetuses and newly-born animals than in those of adults; it apparently has the same importance for the growth of the fetus as does, for instance, phosphorus. They believe that during childhood, while active growth is going on, the arsenic received from the mother, and that later taken in with the food, is utilized in body-building. At puberty, however, an excess of arsenic begins to accumulate; the uterine glands begin to functionate, and to store up this excess, until a sufficient concentration is reached for it to act as a poison. The entire endometrium is affected, the ordinary histologic picture of arsenic poisoning being produced—desquamation of epithelium, fatty degeneration, transudation paralysis of vessel walls, with dilatation of the vessels and escape of blood. In order to determine if the presence of arsenic in the endometrium would have any inhibiting effect on impregnation, the authors investigated the action of living spermatozoa when brought in contact with arsenic solutions on the warm stage of the microscope. They found to their astonishment that such solutions up to 1 per cent. strength (much stronger than is ever present in the endometrium) not only do not have any deleterious action on spermatozoa, but rather seem to increase their activity. In conclusion, the authors state that they consider their experiments so far as suggestive rather than conclusive, and that they merely wish to indicate that this arsenic-storing function of the uterine glands may be one of the numerous factors concerned in the production of the complex phenomenon of menstruation.

## DERMATOLOGY

---

 UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

EMERITUS PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

AND

MILTON B. HARTZELL, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

---

**A Cryptogamic Parasite Found in a Dermatosis of the Type of Pityriasis Rosea.**—DU BOIS (*Annales de Dermatologie et de Syphiligraphie*, 1912, No. 1) reports the finding of a cryptogamic parasite in three cases of a cutaneous disease, one of which was of the type of the pityriasis rosea of Gibert, and the other two resemble varieties of this affection. The parasite consisted of spores of variable size grouped in clusters, without mycelia, in the orifices of the follicles. It did not grow in any of the ordinary media, and was not inoculable. In several of its characters it resembled the microsporon described by Vidal as the cause of pityriasis circinata. Du Bois believes further research will demonstrate its presence in all cases of pityriasis rosea, of which it is the probable cause. He proposes to name it "microsporon dispar."

---

**Bullous Antipyrine Eruptions of the Buccal Cavity.**—NICOLAS and MOUTOT (*Annales de Dermatologie et de Syphiligraphie*, 1911, No. 11), reporting a case of bullous eruption in the buccal cavity due to the ingestion of antipyrine, especially call attention to the possibility of such eruptions being limited exclusively to this region, and to the difficulties which may surround the diagnosis under such circumstances. The first symptoms, which may appear within a few minutes after the ingestion of the drug, but usually not until from three to six hours have elapsed, are a bright carmine redness of the mucous membrane, with more or less swelling, pain, and abundant salivation. After a period varying from a half-hour to two or three days, bullæ appear which rupture after a time, leaving a superficial lesion. Owing to the pain which accompanies the eruption movements of the tongue and jaws are difficult, and there is more or less dysphagia. Although, as a rule, there are no general symptoms, moderate elevation of temperature, dyspnea, vertigo, and vomiting have been observed in some cases.

---

**Skin Changes in Leukemias.**—H. H. HAZEN (*Jour. Cutan. Dis.*, October, 1911) refers to the group of lymphomata involving the skin (which includes leukemia and pseudo-leukemia, lymphosarcomatosis, lymphodermia perniciosa, mycosis fungoides, and chloroma and myeloma). Mycosis fungoides is an aleukemic lymphomatosis and may become leukemia. Reference is made to the "serum reaction" lately discovered by Joltrain and Brin and described by de Beourmann and Verdun which may possibly clear up the relationship. Hazen thinks that the skin lesions of leukemia may probably be compared with the nodules of internal organs met with in splenomyelogenous leukemia.

**Bullous Eruption Associated with Appendix Abscess.**—J. H. SEQUEIRA (*Brit. Jour. of Derm.*, September, 1911) reports the case of a boy, aged three years, who showed numerous blebs on upper and lower extremities, the attack lasting a week, the blebs drying up. A second similar attack, and again a third attack occurred. The lesions suggested a beginning dermatitis herpetiformis. The child was now suddenly taken ill with abdominal pain, and within twenty-four hours was operated upon and a gangrenous perforated appendix found. The blebs on the skin disappeared in a week without any treatment.

**Treatment of Acne by Vaccines.**—MORRIS AND DORE (*Brit. Jour. of Derm.*, October, 1911) quoting Engman's experience and method state that from their own observations they were not able to agree with Engman in regarding "acne bacillus vaccine as one of the most brilliant therapeutic agents in dermatology, comparable in its effects to that of antitoxin on the diphtheritic membrane." They were not able to claim more for the vaccine therapy in acne than that it is a useful adjuvant of the ordinary forms of treatment. There was no evidence that it was capable of inducing true immunity.

**Seven Hundred Consecutive Cases of Tinea Capitis.**—H. M. SCOTT, of London (*Brit. Jour. of Derm.*, October, 1911), states that these cases were seen at the London Hospital, 405 being boys and 295 girls. Of the 700 cases (all examined by the microscope and the fungus demonstrated) 628 were examples of microsporon ringworm and 72 were of endothrix ringworm. The most common ages were from the sixth to the eighth years. The treatment was by the Röntgen rays, the written consent of the parents being first obtained. As a routine measure the whole scalp was treated, five-exposure method of Kienbock as modified by Adamson being employed. Out of 3000 cases of tinea capitis treated at the Hospital no single instance of permanent alopecia occurred.

**Treatment of Erysipelas.**—T. PONTANO (*Policlinico, Rome*, No. 1, 1912) states that in two and one-half years in the Polyclinic, over 1000 cases of this disease were treated, 87 of whom died, but in only 47 cases was erysipelas responsible. The mortality from erysipelas is about 8 per cent. and chiefly in aged or debilitated persons. The various well-known measures for the treatment seem to have been of little value. Hot compresses of physiological salt solution, frequently renewed, reduced the heat and pain as much as the remedies tried, but did not affect the course of the disease.

**A Case of Phenol (Carbolic Acid) Gangrene.**—F. BUCKMINSTER (*Jour. Amer. Med. Assoc.*, January 13, 1912) reports a case of an elderly man, who for a slight bruise and abrasion due to a railway accident, applied an ordinary phenolized petrolatum. After a few applications the tissues broke down into a progressively enlarging gangrenous ulcer, the lesion being upon the leg two inches below the patella. It was cleaned out and treated with hydrogen peroxide and tincture of iodine; healed but again broke down, and now indicated malignancy. At the end of several months' treatment, x-ray applications finally caused healing.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME  
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT;  
SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

**The Formation of Pigment.**—SCHULTZ (*Jour. of Med. Research*, April, 1912, xxvi, No. 1) publishes an interesting study of pigment formation by the dermal chromatophores, from a case of mycosis fungoides, in which the inflammatory process, of low grade, had given origin to a large number of new chromatophores in the subepidermal tissues. Thanks to these, the process of pigment formation could be studied in all its phases. As to the origin of the chromatophore, Schultz considers that no doubt can exist of its mesoblastic origin, to which most readers will agree. He finds this difference between the chromatophores and other mesodermal connective tissue cells, that the former are never seen to form fibrils, and that this is not fortuitous but indicates that the formation of pigment is a special function undertaken by the cell, which thus is freed from the necessity of performing the function of fibril formation. Schultz considers that the pigment is not derived from hemoglobin, nor from the cytoplasm alone, nor is it a degeneration in the ordinary sense of the word; rather it is a definite extension of chromatin from the nucleus into the cytoplasm, and this chromatin takes the staining reactions of nuclear substance, and becomes transformed into pigment; in this transformation of the extruded chromatin into pigment, Schultz thinks the cytoplasm plays a part, either by chemical or catalytic action; and he thus considers that the pigment is a product of nuclear material, and that this nuclear material must not be considered to be cast off as the result of a degenerative process. Those appearances in chromatophores which might be cited as implying degeneration, such as a partite nucleus, Schultz considers to be merely the signs of senescence in a cell that has fulfilled its life-purpose in the usual way.

**Experimental Measles in Monkeys.**—LUCAS and PRIZER (*Jour. of Med. Research*, April, 1912, xxvi, No. 1) have succeeded in producing measles in monkeys by the inoculation, intracerebrally and intraperitoneally, of blood serum from a patient thirty-six hours after the initial rise of temperature and six hours before the appearance of the rash. The inoculated monkeys, after a definite incubation period of six days in one case, showed systemic signs, and on the tenth day Koplik spots could be recognized (this for the first time); during the acute stage of the disease erythema of the face and forehead were noticed, but no more characteristic rash. During the preëruptive period a leukopenia was demonstrated which involved polymorphonuclears, lymphocytes and large mononuclears.

**A New Anaerobic Bacillus in Typhoid Stools.**—**LORIS MELIKOV** (*Compt. Rend. de la Soc. de Biol.*, 1911, lxx, No. 19) publishes his results from growing typhoid fecal matter in liquid medium made of bile, bouillon, and white of egg. From this, at the end of two or three days, subcultures in glucose are made and fine transparent colonies, appear which consist of short bacilli with rounded ends, becoming longer and bent, even curved in older cultures, gram-positive, and non-motile. They grow only at 37° C. and anaërobically, and are proteolytic. The organism is virulent for guinea-pigs, but loses virulence rapidly. Animals dead 12 to 24 hours after inoculation show tumefaction and ulceration of the lymph follicles and Peyer's patches. The organism has not yet been found in stools from other than typhoid patients, and gives positive agglutination with the serum of those suffering from typhoid. It may be that this is the actual agent in the production of typhoid fever.

**Pneumococcus Influenza.**—The statement that there is no influenza without the influenza bacillus is again denied by **C. LEEDE** (*Zeits. f. Hyg. u. Infektionskrankh.*, 1912, Band lxxi, Heft 3), who produces a series of cases to that end. Four years ago Curschmann published 77 cases from 49 of which the influenza bacillus was not obtained, while the pneumococcus was present in so great numbers that he considered it the causative agent. Observer after observer came forward with cases whose contagiousness, apart from their clinical symptoms, spoke for the diagnosis of influenza, yet whose bacteriological examinations showed pneumococcus to be the prevailing germ. Not that pneumococcus was the only organism, for in some cases, not pneumococcus, but streptococcus and staphylococcus were found, and sometimes combinations of these. There are cases that resemble typhoid fever, whose respiratory signs and onset are indicative of influenza, yet whose blood cultures show pneumococcus. In fine, Leede brings forward more cases to show that influenza, as known to the practitioner is a symptom complex, that may be excited by different bacteria, rather than a specific disease due only to the influenza bacillus. Of these different bacteria, the pneumococcus is the most important, and it is able to set up different degrees of sudden infection, now true pneumonia, now a typhoid-like attack, now a short febrile attack, often designated influenza. Leede futher points out that the pneumococcus may attack the bowel giving a colitis at times ulcerative, like that known in true influenza.

**The Detection of Horse Flesh in Sausages.**—For long enough the comic papers have depicted the sausages proclaiming their origin by moving up on the platter to fill the gap made by removal of the first of the row: this homely viand gains one step in the direction of becoming articulate by the work of **G. SEIFFERT** (*Zeits. f. Hyg. u. Infektionskrankh.*, 1912, Band xxxi, Heft 3), who points out the accuracy of the fixation of complement test in the detection of adulteration of sausages by horseflesh.<sup>1</sup>/<sub>2</sub> He uses rabbit-serum, of which <sup>1</sup>/<sub>10</sub> c.c. gives a reaction with horse serum in a dilution of 1 in 20,000 within one minute. The test is accurate for raw, cooked, and smoked horseflesh as well as that treated by ether and antiformin in most minute quantities, while controls with beef and human serum remain negative,



**The Local Effect of Orchitis in Mumps.**—So rarely is pathological effect of mumps upon the testis to be observed post mortem that it is interesting to note that HALL (*Virchow's Archiv.*, 1912, Band ccvii), obtained a case in a youth, aged eighteen years, who had suffered from mumps and orchitis a year before his death. There was visible atrophy of the testis; microscopically, there was definite atrophy of the tubules, with a diffuse fibrosis.

**Trichiniasis.**—M. ROMANOVITCH (*Ann. de l'Inst. Pasteur*, May 25, 1912, xxvi, No. 5), although for reasons given adhering to the old nomenclature, points out that in future, following Raillet, we should call the trichina the *Trichinella spiralis*. The female penetrates the mucosa of the bowel, but does not pass the muscularis mucosæ; it deposits its larvæ in or close to lymphatic vessels, whence they are carried to the blood stream; considering this, Romanovitch thinks that where suspected meat has been eaten, it would be possible by a daily examination of the blood, to recognize the spread of the infection. Karyokinetic figures are seen frequently in the immediate neighborhood of the invaded lymphatics. The larvæ perish rapidly in the serous cavities; the muscle is, of course, its place of choice. Romanovitch points out that in traversing the intestinal mucosa, the trichina deposits as it goes the bacteria with which its surface is covered, whence arise the polymicrobial secondary infections which occur in cases infected by the worm. He appears scarcely willing to say that fever, abscess-formation, and septicemia are due to infections arising in this way, but thinks it would be hard to prove the contrary assertion. The serum of infected rats and guinea-pigs becomes toxic, as does the urine of highly infected animals; in ordinary infections, this toxicity may appear as early as the ninth day and may last a month; it is iso- and hetero-toxic. The search for specific antibodies in the serum has not succeeded, either in the direction of precipitins or fixation of complement. As antigen Romanovitch employed aqueous extract of measly muscle. As had been noted of others, definite reinfection was found to occur, so that it seems quite impossible to immunize animals against the parasite. Finally, no treatment, preventive or abortive, has yet been found. Salvarsan does not appear to exert any action whatever upon the larvæ. Atoxyl proved similarly inefficacious.

---

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only with the distinct understanding that they are contributed exclusively to this JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translate at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, provided the request for them be written on the manuscript.

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

# CONTENTS

## ORIGINAL ARTICLES

- A Study of the Endocardial Lesions of Subacute Bacterial Endocarditis, with Particular Reference to Healing or Healed Lesions; with Clinical Notes.** . . . . . 313  
By E. LIBMAN, M.D. Professor of Clinical Medicine, Columbia University, New York; Associate Attending Physician and Associate Pathologist Mount Sinai Hospital, New York.
- Glomerular Lesions of Subacute Bacterial Endocarditis** . . . . . 327  
By GEORGE BAEHR, M.D., Assistant in Pathology, Mount Sinai Hospital, New York.
- The Relation of Hypertension to Urinary Excretion** . . . . . 330  
By CHARLES H. LAWRENCE, JR., M.D., Assistant Visiting Physician, Massachusetts General Hospital, Boston, Mass.
- The Brain Lesions Produced by Electricity as Observed after Legal Electrocution** . . . . . 341  
By EDWARD ANTHONY SPITZKA, M.D., Director and Professor of General Anatomy, the Daniel Baugh Institute of Anatomy of the Jefferson Medical College, and HENRY E. RADASCH, M.D., Assistant Professor of Histology and Embryology, Jefferson Medical College of Philadelphia.
- Hospitals and Typhoid Carriers** . . . . . 347  
By JOHN W. BRANNAN, M.D., New York.
- The Therapeutic Use of Vaccines in Typhoid Fever** . . . . . 350  
By JAMES G. CALLISON, M.D., Pathologist, Manhattan Eye, Ear, and Throat Hospital, New York.
- Stenosis of the Duodenum: A Statistical Study, with the Report of a New Case** . . . . . 360  
By JAMES M. ANDERS, M.D., LL.D., Professor of Medicine and Clinical Medicine in the Medico-Chirurgical College, Philadelphia.
- The Complement-fixation Test in the Differential Diagnosis of Acute and Chronic Gonococcic Arthritis.** . . . . . 369  
By HANS J. SCHWARTZ, M.D., Instructor in Clinical Pathology and Clinical Instructor in Dermatology in the Cornell University Medical School, New York.
- A Critical Commentary on the Free Eye Infirmary, with Suggestions as to Reforms in Ophthalmic Hospitals, Dispensaries, and Schools. A Compilation from Correspondence and Observation.** . . . . 386  
By H. V. WURDEMAN, M.D., Editor "Ophthalmology;" Associate Editor "Ophthalmic Record;" Formerly Professor of Ophthalmology, Marquette University; Chairman Section on Ophthalmology, American Medical Association, 1901, etc., Seattle, Washington.

<b>The Treatment of Locomotor Ataxia</b> . . . . .	398
By EDWARD LIVINGSTON HUNT, M.D., Associate Consulting Neurologist, St. Luke's Hospital, New York.	
<b>Tuberculin Therapy in Surgical Tuberculosis</b> . . . . .	403
By THOMAS WOOD HASTINGS, M.D., Professor of Clinical Pathology in the Cornell University Medical College, New York.	

---

## REVIEWS

Recent Methods in the Diagnosis and Treatment of Syphilis. (The Wassermann Reaction and Ehrlich's Salvarsan, "606.") By C. H. Browning, M.D., and Ivy McKenzie, M.D. . . . .	427
Health and Medical Inspection of School Children. By Walter S. Cornell, M.D. . . . .	428
Tumors of the Jaws. By Charles Locke Scudder, M.D. . . . .	429
Diseases of the Stomach. By Max Einhorn, M.D. . . . .	430
The Diseases of Infants and Children. By Edmund Cautley, M.D. Cantab, F.R.C.P. Lond. . . . .	431
The New Physiology in Surgical and General Practice. By A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. . . . .	433
Juckende Hautleiden. By Dr. S. Jessner. . . . .	433
Ueber Neurorezidive nach Salvarsan und nach Quecksilber Behandlung. By Dr. J. Benario . . . . .	434
Ophthalmic Year Book for 1911. Edited by Edward Jackson, M.D., Theodore B. Schneideman, M.D., and William Zentmayer, M.D. . . . .	435
Fourth Scientific Report of the Investigations of the Imperial Cancer Research Fund. By Dr. E. F. Bashford. . . . .	436
Clinical Lectures on the Acute Abdomen. By William Henry Battle, F.R.C.S. . . . .	437
Dental Anesthetics. A Text-book for Students and Practitioners. By Wilfred E. Alderson, M.D. (Durham), M.S., B.Hy., D.P.H. . . . .	437
Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., assisted by Leighton F. Appleman, M.D. . . . .	438

---

## PROGRESS OF MEDICAL SCIENCE

### MEDICINE

#### UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

A Test of Gastric Motility . . . . .	439
Ehrlich's Aldehyde Reaction in Circulatory Diseases . . . . .	440
Experimental Eosinophilia after Intraperitoneal Injection of Protein and the Relation of Eosinophilia to Anaphylaxis . . . . .	440

Action of Salvarsan in Anthrax . . . . .	441
Chemistry and Toxicology of Ascarides . . . . .	441
Deodorizing Excreta . . . . .	442
Leukocytic Inclusions in Scarlatina . . . . .	442
The Establishment of Treponema Pallidum as the Causative Agent of Syphilis, and the Cultural Differentiation between this Organism and Certain Morphologically Allied Spirochetæ . . . . .	443

## SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

Operation for Perforated Stomach and Duodenal Ulcers . . . . .	444
Surgery of Horse-shoe Kidney . . . . .	445
Hydrarthrosis in a Horse-shoe Kidney . . . . .	446
The Experimental Production of Basedow's Disease . . . . .	446
Orthopedic Resection of the Pelvis of the Kidney for Hydrarthrosis, with Intermittent Crises . . . . .	447
Surgical Pathology of the Stomach and Duodenum . . . . .	447
Observation on the Radical Cure of Hernia . . . . .	447
An Experimental Contribution to the Formation of Arterial Capillaries in the Kidneys . . . . .	448
Duodeno-jejunal Occlusion as a Separate Condition . . . . .	449

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

The Effects of Pressure Lowering Drugs and Therapeutic Measures on Systolic and Diastolic Pressure in Man . . . . .	449
The Treatment of Scarlet Fever with Injections of Serum from Convalescents . . . . .	450
The Secondary Effects of Harmonal . . . . .	451
The Hypodermic Injections of Iron and Arsenic in Secondary Anemia . . . . .	451
Neosalvarsan . . . . .	452
By-effects of Harmonal . . . . .	452
The Treatment of Acute Endocarditis due to Streptococcus Viridans . . . . .	452
The Serum Treatment of Typhoid Fever . . . . .	452
Untoward By-effects of Harmonal . . . . .	453
The Treatment of Tetanus with Magnesium Sulphate . . . . .	453

## PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

The Use of Salvarsan in Hereditary Syphilis . . . . .	454
The Treatment of Acute Spastic Bronchitis in Early Childhood . . . . .	454
Studies in the Nutrition and Digestion of Infants . . . . .	455
Inclusion Bodies in the Blood in Scarlet Fever . . . . .	456

**OBSTETRICS**

UNDER THE CHARGE OF

**EDWARD P. DAVIS, A.M., M.D.**

The Diagnosis of the Pernicious Nausea of Pregnancy . . . . .	457
The Needless Interruption of Maternal Nursing. . . . .	457
Icterus Neonatorum . . . . .	457
Parturition during Adolescence . . . . .	458
Sugar in the Blood in Pregnancy, Labor, the Puerperal State, and Eclampsia . . . . .	458
The Differential Diagnosis of Pregnancy . . . . .	458
Changes in the Symphysis and Other Pelvic Joints in Parturient Patients . . . . .	459
Pregnancy and Double Pyosalpinx . . . . .	460
Death of the Child from Rupture of the Umbilical Vessels during Labor. . . . .	460
Ovarian Pregnancy . . . . .	461
The Treatment of Puerperal Sepsis by Cultures of Lactic Bacilli . . . . .	461

**GYNECOLOGY**

UNDER THE CHARGE OF

**JOHN G. CLARK, M.D.**

Ovarian Transplantation . . . . .	462
Is Laparotomy Indicated in Peritoneal Tuberculosis? . . . . .	462
Spontaneous Cure of Cancer . . . . .	463
Treatment of Metritis . . . . .	464

**OPHTHALMOLOGY**

UNDER THE CHARGE OF

**EDWARD JACKSON, A.M., M.D.,**

AND

**T. B. SCHNEIDEMAN, A.M., M.D.**

Keratitis Punctata Subepithelialis . . . . .	465
Pathology of Superficial Punctate Keratitis . . . . .	465
Treatment of the Early Stages of Senile Cataract . . . . .	466
Sclerectomy with Iridectomy in Chronic Glaucoma: Lagrange Operation . . . . .	466
The Size of the Blind Spot and its Distance from the Point of Fixation in Emmetropia . . . . .	466
Failure in Strabismus Operations . . . . .	466
Dust-like Opacities in the Vitreous . . . . .	467

**PATHOLOGY AND BACTERIOLOGY**

UNDER THE CHARGE OF

**JOHN McCRAE, M.D., M.R.C.P.**

Immunity Transmission from Mother to Offspring . . . . .	467
A Suggested Explanation of the Apical Lesion in Tuberculosis . . . . .	468

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

SEPTEMBER, 1912

---

ORIGINAL ARTICLES

A STUDY OF THE ENDOCARDIAL LESIONS OF SUBACUTE  
BACTERIAL ENDOCARDITIS, WITH PARTICULAR  
REFERENCE TO HEALING OR HEALED  
LESIONS; WITH CLINICAL NOTES.

BY E. LIBMAN, M.D.,

PROFESSOR OF CLINICAL MEDICINE, COLUMBIA UNIVERSITY, NEW YORK; ASSOCIATE ATTENDING  
PHYSICIAN AND ASSOCIATE PATHOLOGIST, MOUNT SINAI HOSPITAL, NEW YORK.

DURING the last ten years I have been enabled to study an unusually large number of cases of subacute bacterial endocarditis. Particularly in the last few years I have become impressed with the great frequency of the condition (in 1911 I saw 27 cases). Altogether I have had the opportunity of studying at least 89 cases. Blood cultures were made in 75 of 78 active cases—by this I mean cases in what I call the bacterial stage. The other 3 cases were typical clinically; 1 passed out of observation and the other 2 died, autopsies not being obtainable.

Organisms were recovered from the blood of 73 of the 75 cultured cases. In 71 cases the cocci characteristic of the disease were obtained,<sup>1</sup> and in 4 the influenza bacillus. The symptoms and lesions found in the latter group were practically the same as those found in the former, except that thus far the glomerular lesions in the coccus cases have not been discovered in the kidneys of the influenzal cases that have come to postmortem examination.

I shall not now discuss the proper classification of the cocci found in this disease, leaving that for another publication. I shall

<sup>1</sup> Libman and Celler, AMER. JOUR. MED. SCI., 1910, cxi, 516, and Trans. Assoc. Amer. Phys., 1910.

simply say here that the cocci we have obtained seem to be identical with those found by other investigators.<sup>2</sup> Until their exact status is determined we shall refer to them as the "endocarditis cocci" or "coccus." Studies by Rosenow indicate that the organisms are derived from pneumococci, a view also discussed in the paper by Celler and the writer.

There were 2 supposedly active cases in which the blood cultures were negative. In the former five cultures were made in a variety of ways in our laboratory, and one in another, all being negative. This patient died at another hospital, and characteristic lesions were found in the heart, with cocci in the vegetations. These cocci were not studied, but I have no hesitation in putting down the case as one belonging in the group of subacute bacterial endocarditis. In the other case two cultures were made, neither very satisfactory. This case died and there was no autopsy made, but the clinical picture was definite.

The term "subacute bacterial endocarditis" I have adopted instead of the older terms: "chronic ulcerative endocarditis," "chronic malignant endocarditis," "chronic infectious endocarditis," and "endocarditis lenta" (Schottmüller). I call all cases of endocarditis already proved to be due to bacteria (rheumatism is not so proved) "bacterial endocarditis," and divide the cases into "acute," "subacute," and "chronic," according to their clinical course. When the causative organism in a given case is obtained, I insert the name of the organism for the word "bacterial," thus, "acute streptococcus endocarditis," etc. Many of the cases that belong in the group with which we are dealing last only four to six months, and are therefore certainly subacute and chronic. Some may prefer to apply the term "chronic" to the cases that last over one year.

Besides the 77 active cases, we have observed 11 cases, which I believe belong in the group of subacute bacterial endocarditis, but in which the lesions found were in a healing or healed stage, and in which the lesions were found free from pathogenic bacteria. In 10 of the cases, blood cultures were made during life (in a few anaërobically), and no bacteria were found. In 1 case as many as nine cultures were made during a period of ten months, all with negative results.

There are many viewpoints from which such large material as I have at my disposal could be presented. I shall attempt in the present communication to show that the lesions found in the cases of subacute bacterial endocarditis in which the mitral valve is involved are quite characteristic. I hope to demonstrate that there are three stages in many cases of this disease: the bacterial, the

<sup>2</sup> Libman and Celler, AMER. JOUR. MED. SCI., 1910, cxl, 516, and Trans. Assoc. Amer. Phys., 1910.

bacteria-free healing, and the bacteria-free healed stage. I should also like to point out that at least some of the cases which we have been wont to call "chronic endocarditis with fever" are examples of the healed or healing forms of subacute bacterial endocarditis, for healing from a bacteriological or bacteriological and pathological standpoint does not necessarily mean recovery from a clinical standpoint.<sup>3</sup>

I shall here present my views as briefly as possible and refer to the literature in so far only as is essential. At another time I hope to cover the subject more fully and to discuss the lesions found in other forms of endocarditis. I shall point out for comparison some of the valvular lesions found in infections by the ordinary streptococci, pneumococci, staphylococci, and the gonococcus.

When the mitral valve is involved in cases of subacute bacterial endocarditis (and it is involved in the larger number of cases) there is a tendency for the vegetations to spread up on the left posterior wall of the auricle more than on the valve itself. Often the chordæ tendineæ attached to the posterior flap are covered to a greater or lesser extent by vegetations. Nearly always the anterior flap is also involved, and here the vegetations tend to grow down over the chordæ tendineæ, the involvement of the latter being often extensive. Not uncommonly the chordæ are ruptured, the torn ends at times being massed together by vegetations at the edge of the flap, or the lower ends may be found lying loose near the papillary muscles. The vegetations are yellowish, greenish, pinkish, or reddish in color, and vary much in size in different cases. As they grow older they become firmer and assume a more grayish color.

When the aortic valves are involved the lesions are not usually characteristic and their extent is most variable. There may be only a small vegetation on one or more of the flaps of the valve. On the other hand, there may be enormous green masses that must block the orifice to a greater or lesser extent. The vegetations have a tendency to extend down over the endocardium at the position of the septum membranaceum and over the ventricular aspect of the aortic flap of the mitral valve and down over the chordæ tendineæ. At times they have a stalactite-like appearance. There may develop an aneurysm of the aortic flap of the mitral valve. Ulceration of the aortic valve at times occurs; ulceration of the mitral flaps is rare.

A study of frequency of involvement of the valves, the left auricle, and the chordæ in the hearts from 34 cases of the disease in which the blood cultures were positive during life was made with the following results:

\* Libman, Proc. New York Path. Soc., December, 1911, xi, 118.



Auricle, mitral valve, and chordæ . . . . .	17 cases
Auricle, mitral valve, chordæ, and aortic valve . . . . .	5 "
Auricle and mitral valve . . . . .	2 "
Mitral valve and chordæ . . . . .	1 "
Aortic valve only . . . . .	3 "
Aortic valve, chordæ, and aortic flap of mitral . . . . .	4 "
Mitral valve, chordæ, and aortic valve . . . . .	1 "
Auricle, mitral, and aortic valves . . . . .	1 "
<hr/>	
Total . . . . .	34 cases

The auricle was involved 25 times, the mitral valve 27 times, the chordæ 28 times, and the aortic valve 9 times. The frequency of the involvement of the chordæ and auricle is very striking.

The lesions which we consider so characteristic of this group of cases we have not found in a large series of cases of acute endocarditis (58 in number) due to the streptococcus, pneumococcus, and the staphylococcus. In our own cases of acute gonococcus endocarditis we have not met with similar lesions. But I have, through the kindness of Drs. Asch and Humphries, of the German Hospital, seen one case of gonococcus endocarditis, apparently of only three weeks' duration, in which the lesions resembled those seen in the group of cases under discussion. The symptoms seen in the typical cases of subacute bacterial endocarditis were not present nor were the characteristic glomerular lesions found in the kidneys.

And as, in the group of 34 cases just tabulated above, only 1 was due to the influenza bacillus and the other 33 to the endocarditis coccus, the lesions must be considered characteristic of infection by these cocci. There are occasional notes in the literature on such lesions in cases of bacterial endocarditis, particularly by Osler<sup>4</sup> and Harbitz.<sup>5</sup> These will be discussed in the fuller paper which will appear later.

After I had made these observations I found (in 1909) lesions in the heart of a man in whose case a clinical diagnosis of chronic nephritis and uremia had been made, which appeared to me to represent the healed form of the lesions I had previously found in cases of infection by the endocarditis cocci. There were extensive lesions on the wall of the auricle in a state of organization, and the chordæ tendineæ attached to the anterior flap were found torn, thickened, fibrous, and in part calcareous. Bacteria were not present. My opinion that these were the healed lesions of subacute bacterial endocarditis (in all probability due to the cocci) was confirmed recently by Dr. Baehr's<sup>6</sup> studies of the kidneys in all the material we have in the museum from cases of bacterial infection of the heart valves.

<sup>4</sup> British Med. Jour., 1885, i, 467, 522, 577, 607; Practitioner, 1893, p. 181; Quart. Jour. Med., ii, 219.

<sup>5</sup> Om. Endokardit, 1897, Christiana; Deutsch. med. Woch., 1899, xxv, 121.

<sup>6</sup> Proc. New York Path. Soc., December, 1911, xi, 123; Jour. Exp. Med., 1912, xv, 330.

Dr. Baehr investigated particularly the glomerular lesions described by Loehlein<sup>7</sup> in cases of endocarditis due to the *Streptococcus viridans* of Schottmüller,<sup>8</sup> which organism seems to correspond to the cocci found in our subacute cases. Dr. Baehr studied the kidneys of 25 cases of endocarditis due to the endocarditis coccus ("*Streptococcus viridans*" or "*Streptococcus mitis*") which were still in the bacterial stage, and found the lesions described by Loehlein in 23. In 2 other cases, 1 an infection by the influenza bacillus and the other the case of gonococcus infection before mentioned (with rather acute course, but with endocardial lesions like those in the coccus case), the lesions were absent.<sup>9</sup> In the kidneys of 54 cases of endocarditis due to the ordinary streptococci, staphylococci, the pneumococcus, and the gonococcus no such lesions were found. The lesions must therefore be considered characteristic of infections of the heart valve by the endocarditis coccus.

In the kidneys of the case which I have just mentioned, which I believed at the time the case came to postmortem examination represented a spontaneously healed case (from the bacteriological and pathological standpoints), the characteristic glomerular lesions were found. After observing this case I again looked over my collection of hearts from cases of subacute bacterial endocarditis, and was surprised to find how often there is a tendency to healing of at least part of the lesions. In a number of cases I found that the upper part of the auricular lesion was already organizing or was organized, while other parts of the lesions were active and filled with bacteria. I also found a tendency to calcareous infiltration in chordæ tendineæ which were covered by vegetations. And even in extensive vegetations on the aortic valve, which on the whole appeared to be quite active, marked calcareous deposits could be found. It was of the greatest interest to observe the transitions between the lesions present in active cases and the lesions we were beginning to find in the cases which I believed to represent healed cases of the disease in question. Including the case mentioned above (Case I) we have now studied the lesions in 11 cases in the last-mentioned group.

CASE II.—The clinical diagnosis was chronic endocarditis, chronic nephritis, uremia. In the heart there was an organized lesion of the wall of the left auricle. The chordæ tendineæ were thickened, deformed, some were shortened, some torn. One blood culture was made during life, which gave a negative result. The lesions were bacteria-free; glomerular lesions were found.

CASE III.—A case considered to be possibly a case of subacute bacterial endocarditis in which the bacterial infection was no

<sup>7</sup> Med. Klin., 1910, xi, 375.

<sup>8</sup> Münch. med. Woch., 1910, lvii, 617.

<sup>9</sup> Since Dr. Baehr wrote his paper, Dr. Thalhimer has studied with me the lesions in another subacute case due to the influenza bacillus. The glomerular lesions were not present.

longer present. Death was due to exhaustion from anemia and to an embolic aneurysm of the femoral artery. Three blood cultures were made, with negative result. At autopsy there were characteristic lesions of the left auricle and the chordæ, partly organized. There were few poorly staining cocci in the non-organized part of the lesions; they could not be cultivated. Characteristic glomerular lesions were found.

CASE IV.—The clinical diagnosis was chronic endocarditis and chronic nephritis. Characteristic lesions in healing state were found post mortem, bacteria-free. There was no blood culture during life. Glomerular lesions were found.

CASE V.—This case is of particular interest. I had the opportunity of personally observing this patient last summer, in the service of Dr. J. Rudisch. He was a type of case usually termed "chronic endocarditis, with fever." Certain clinical phenomena led me to believe that the case was one of bacterial endocarditis in which bacteria were no longer present, and that the continuance of the clinical phenomena was due to the fact that there was present a large calcareous mass on the aortic valve from which pieces were continually breaking off, the calcareous mass representing the attempt at healing of a large mass of vegetations. At autopsy the conditions were as suspected during life. There was a large calcareous mass present, and there was some ulceration of the valve flaps. As the lesions on the aortic valve are not characteristic in subacute bacterial endocarditis, as those of the mitral usually are, I could not put this case in the group until Dr. Baehr found typical healed glomerular lesions. Two blood-cultures were made in this case; both remained sterile. The masses on the valve were bacteria-free.

CASES VI and VII.—When I thus found that a case with the clinical picture of "chronic endocarditis with fever" could really be a case of bacteria-free subacute bacterial endocarditis I had the kidneys from two other such cases examined. One case had calcareous masses on the aortic valve, an aneurysm of the mitral valve, embolic aneurysm of the iliac artery, and a branch of a renal artery.<sup>10</sup> A few of the chordæ tendineæ attached to the anterior mitral flap showed organized vegetations. Three blood cultures were negative in this case. The lesions post mortem were free from bacteria, and typical healed glomerular lesions were found by Dr. Baehr. The other case presented at postmortem examination calcareous masses on all three flaps of the aortic valve, with some ulceration of the valve. There was also an aneurysm at the position of the membranous septum. Death was due to cerebral embolism. Three blood cultures in this case

<sup>10</sup> It is interesting to note, in view of the clinical remarks appended, that when I looked up the history of this patient, who was in the hospital seven years ago, the house physician had made a note that there was facial pigmentation and a palpable spleen.

revealed no bacteria. Healed glomerular lesions were easily found. It is of great interest to compare the heart in this case with another in my collection in which there are vegetations on all three flaps of the aortic valve. Although there are cocci present, and they were still to be found in the blood at the time of death, distinct calcareous impregnations are present. It is easy to see that this heart might easily look like the one from the bacteria-free case if the process of calcification were further advanced.

CASE VIII.—This case was suspected of being in the bacteria-free stage of subacute bacterial endocarditis. One blood culture was made, with negative result. There were slight organized lesions of the aortic valve. There was a granular lesion of the left auricle and the chordæ tendineæ showed typical changes, but in an organizing or organized condition (histological studies not complete). There were no bacteria in the lesions.

CASE IX.—This case was also strongly suspected clinically of being one of subacute bacterial endocarditis, that had become bacteria-free. The cause of death appeared to be a cerebral embolism. The autopsy showed a slight healed lesion of the posterior flap of the mitral valve. The chordæ tendineæ attached to this flap showed apparently organized vegetations (histological examination not completed). The changes in the anterior flap were like those seen in active bacterial cases of disease; the chordæ tendineæ were matted together at their attachment to the valve, and some of them were torn across. All these lesions appeared to be organized. There was one finger-like vegetation attached to the cusp, which hung down into the ventricle as far as the insertion of the chordæ into the papillary muscle. This vegetation did not seem to be as old as the others. The aortic flaps showed very small vegetations, and one cusp was slightly ulcerated. Three blood cultures were made, all with negative results. The lesions were found bacteria-free; glomerular lesions were found.

CASE X.—This case was also suspected clinically of being one of the remarkable instances of healing endocarditis when the patient was in the hospital in December, 1911. A blood culture taken at that time showed no growth. He returned in March, 1912, with an embolism (embolic aneurysm?) of the right brachial artery. Two blood cultures were negative. At the autopsy the usual lesions were found that are characteristic of subacute bacterial endocarditis when the mitral valve is attacked. The lesions seemed to be nearly if not entirely organized (examination not finished). There was one unusual lesion, an old ulceration of the posterior flap of the mitral valve. The vegetations were found bacteria-free. The heart blood contained saprophytic bacteria only. Glomerular lesions were easily found.

CASE XI.—This case was observed much longer than any other case in this group. The patient was constantly seen for nearly

ten months, and was several times under observation in the hospital. In all nine blood cultures were made, some being incubated anaërobically (this was also done in several of the other eleven cases now under discussion). Not a single colony of an organism was found. The man died of anemia, exhaustion, and decompensation. At the autopsy there were found extensive deposits of calcareous, fibrous, and thrombotic material on the flaps of the aortic valve. There were perforations of the valves with healed margins; these were clearly due to ulceration. There were also present aneurysms of the sinuses of Valsalva. Spreads of the vegetations proved bacteria-free. Cultures of the heart blood showed the ordinary streptococcus, evidently a terminal or agonal invader. The kidneys showed the typical glomerular lesions all healed.

I wish to digress for a moment here to mention a further finding which to me seems important and to which hitherto no attention has been paid. This patient had the sternal tenderness which I described in an earlier paper<sup>11</sup> as being such a frequent, valuable symptom in subacute bacterial endocarditis, and he had it to an unusually marked degree. I had suspected that it was due to active regeneration in the bone marrow, this being an effort at compensation for the marked progressive anemia so common in the disease. There was another possibility to be entertained, although it was less likely—namely, embolic disease of the bone marrow.

When we performed the autopsy in this last case we were able to obtain bone marrow from the tibia, femur, and sternum. In the femur and sternum and in the middle of the tibia the marrow was dark brownish red in color, and very firm. It is now being studied histologically.

We have then before us 11 cases in which we have every reason to believe that we are dealing with cases in which patients who had a subacute bacterial endocarditis overcame the infecting agent without their having been seen at a time when the infection was still active. In 1 poorly staining cocci were still seen in small numbers in part of the lesions. In 7 of the cases the mitral valve was involved in a way seen practically only in subacute bacterial endocarditis. As 95 per cent. of our active cases were found to be due to the endocarditis coccus, it is fair to assume that nearly all of the 7 cases were due to the coccus. Besides which we have further evidence in the presence of the characteristic glomerular lesions in all of them.

One case had a calcareous mass on the aortic valve and involvement of the chordæ tendineæ in characteristic fashion. The latter lesion is in itself suggestive, and besides this typical glomerular lesions were found.

We have left 3 other cases in which only the aortic valve was

involved and in which large calcareous lesions were found. In all of these we have the proof afforded by the presence of the glomerular lesions that they were, almost surely the result of infections by the endocarditis coccus. And I have pointed out that there are transition stages to these lesions in cases which still have the cocci in the blood during life and in the lesions.

It is of interest to note in the cases with aortic involvement (calcareous masses on the valve) that aneurysms are frequent and that they are of a different type from the bacterial embolic type. One finds aneurysms of the sinuses of Valsalva, the heart wall just below the aortic valve, the aortic flap of the mitral valve, and in the peripheral arteries. All except the last seem to be due to impact by the calcific material on the valve. They are all smooth walled. The peripheral aneurysms seem to be due to the traumatism to the wall inflicted by a piece of lime whipped off from the valve. Some years ago I pointed out that such non-infective embolic aneurysms actually existed.<sup>12</sup>

The question will now be asked, How often does one see a case of subacute bacterial endocarditis in which blood cultures have been positive, become bacteria-free and go on with symptoms due to the changes left in the heart or recover completely? As regards this point, our own experience has been that nearly all the cases in which we found bacteria in the blood and which we could follow went on to a fatal termination, with bacteria still present in the blood. In but few cases did the blood cultures become negative; these patients also soon succumbed. In one case of infection by the influenza bacillus five blood cultures were positive and four later ones were negative. This patient died a couple of months after leaving the hospital, or about four months after the cultures became negative. He left the hospital quite anemic, and died of exhaustion and decompensation. An autopsy was not permitted. Our experience coincides with that of those who have seen large numbers of these cases. The instances of recovery in cases with positive blood cultures will later be cited briefly in the discussion of the literature.

It is curious in view of the facts just stated that there should exist so many cases<sup>13</sup> which must have had a bacterial infection, have recovered from the infection, and have certain clinical pictures from the changes brought about during the infective period. We must assume that in these cases the period of bacterial infection was very short as compared to the cases which we see with bacteria in the blood or very short and very mild. When one sees cases of

<sup>12</sup> Proc. New York Path. Soc., October, 1905, p. 88.

<sup>13</sup> I have seen a number of cases besides those mentioned in the text which I believed to be examples of bacteria-free cases. Some have disappeared from observation. A few I am still following. I believe we will be surprised at the number of such cases that exist and have hitherto not been properly interpreted.

the disease with bacteria demonstrable in the blood go about for weeks with hardly any symptoms it is not difficult to believe that some patients with a mild or short infection may not feel sick enough to ask for medical attention or present such mild clinical pictures that they are not put to bed. That the infection in such cases is a shorter one is also suggested by the study of the glomerular lesions. They were found to be much more abundant in cases in which cocci had been found in the blood than in those in which they were never demonstrated. It is not my purpose in this communication to discuss at length the clinical pictures presented by the cases with healing or healed lesions. A sufficient number of cases has not yet been collected to give us a clear idea of the complete course of such cases. It will be important to determine how long people with this condition can live, and whether any of them after the bacterial infection is over can live for many years with no other symptom than those they had from their original valvular lesion before the infection was superimposed. My own data are too few to give any definite facts. But two observations are of some value. One case (Case XI) was observed in a bacteria-free condition almost ten months. In Case X a transfusion prolonged the patient's life. I have another case under clinical observation who has but few symptoms, who is in no worse condition today (perhaps even better) than he was ten months ago.

As far as the data which I have thus far at my command go they indicate that the cases with healing or healed lesions present the following clinical pictures:

1. They go on to have a nephritis and die of uræmia.
2. They present the picture corresponding to what we have been wont to call "chronic endocarditis with fever" (that is they have a valvular lesion, more or less fever from time to time, usually low, occasional petechiæ,<sup>14</sup> occasional joint symptoms, and embolisms). Some of these cases closely resemble cases in which bacteria are demonstrable in the blood. The differences will be discussed when I have more material. Some of these patients are pale and some more or less pigmented (see below).
3. Some of these cases present a clinical complex that appears to have been entirely overlooked. The striking feature is a peculiar diffuse brown (sometimes quite dark) color of the face. The rest of the body may show some pigmentation. There is evidence of a valvular lesion, there is more or less anemia, usually a palpable spleen, and usually also tenderness of the lower sternum.<sup>15</sup> The patients feel weak and do not sleep well. Petechiæ occasionally

<sup>14</sup> My investigations go to show that purpuric eruptions occur particularly in the cases with calcific masses in the valves.

<sup>15</sup> This symptom will be more fully discussed in a separate publication, as will also the changes in the urine.

occur. There is temperature from time to time, but usually low. Erythrocytes are found in the urine in some of the cases. The subsequent history of such cases is not yet known; one case died with symptoms of cerebral embolism. I wish particularly to emphasize the curious change in the color of the face. It will, I am sure, be of great importance in the recognition of some of the cases with healing or healed lesions. Since I have observed it in such cases I have looked for it in cases with bacteria in the blood. And now, to my surprise, I find that while the faces of most of the cases are sallow, or of a rather white color, some develop a certain amount of brown or *café-au-lait* color.

4. They may go on with more or less anemia, and suffer from that and from decompensation.

I would like now to note a few of the important symptoms that occur in the bacterial cases and state what my experience is as regards them in the cases in which the infection has been overcome:

1. Fever: This is found in all of the non-bacterial cases that we have observed, but it is a less marked feature and the temperatures are low for much longer periods. In an earlier paper I have drawn attention to the fever which occurs in cases of chronic endocarditis without demonstrative bacteriemia.<sup>16</sup> At that time I made the following remarks: "There are many cases of chronic endocarditis with fever without demonstrative bacteriemia. In some cases causes for the fever may be found elsewhere in the body. If no cause can be found the acute symptoms may be due possibly to organisms not to be cultivated by our present methods. I have suspected that in some cases with irregular fever, at times high, and recurring from time to time, the temperature may be due to the discharge into the blood current of bits of thrombotic masses or old vegetations." Bock<sup>17</sup> has recently shown that fever can be produced experimentally by the injection into the blood stream of bacteria-free, chemically indifferent particles.

2. Splenic Enlargement: This symptom seems to persist in the non-bacterial stage. I have reason to suspect that occasionally when the spleen is very large, the clinical diagnosis may appear to be a splenic disorder plus chronic endocarditis. In the bacterial stage, it is well known that the splenic enlargement may be so marked that such cases have been mistaken for cases of Banti's disease or splenic anemia.

3. Pains: These may be just as severe in the bacteria-free cases; the same holds true of joint pains.

4. Painful Cutaneous Erythematous Nodules: These were not observed in the bacteria-free cases except in one case, in which

<sup>16</sup> Libman, Johns Hopkins Hosp. Bull., 1912, p. 222.

<sup>17</sup> Bock, Arch. exp. Path. u. Pharmacol., Band lxxviii, 68, I.



they were a prominent feature during the early period of the observation.

5. Sternal Tenderness: This symptom, on which I lay much stress, is equally frequently met with in both groups of cases. It even seems to be a more marked symptom in the bacteria-free cases. As I have stated in an earlier publication,<sup>18</sup> sternal tenderness may be found even when the hemoglobin is not markedly reduced.

6. Petechiæ: These occur in the bacteria-free cases, but are not as abundant and do not occur so frequently. Purpuric eruptions seem to be a feature rather of some of the bacteria-free cases.

7. Hematuria: This subject needs further investigation. Erythrocytes were found in the urines of those cases of the bacteria-free groups in which they were carefully looked for. Gross hematuria—that is to say, smoky urine—I remember to have seen only once in the cases in the bacteria-free group, and it occurred in that case only during the early part of the period of observation.

Other symptoms, such as the sweats, the blood changes, the gastrointestinal phenomena, etc., will be discussed when more data are available. The facts that I have given show the close resemblance between many of the features in the two groups of cases. It is important that we can recognize at least some of the bacteria-free cases definitely. It will be of great value to search for such cases and to make studies of the serum in them. Complement fixation investigations carried on in connection with such cases may enable us to determine the exact status of the cases classed as chronic rheumatic endocarditis. We may be able to ascertain whether there exist cases that have had the bacterial infection and have completely recovered, being left with the original valvular lesion due to rheumatism.

It will finally be of interest to glance at the literature on the subject of healing of the lesions of subacute bacterial endocarditis. I shall take up at the present time mainly the experience of authors who have had the advantage of having blood cultures made in their cases. I shall not go into the question of the possibility of the healing of acute endocarditis; Herrick<sup>19</sup> has discussed that subject fully.

Litten,<sup>20</sup> Leyden,<sup>21</sup> Osler,<sup>22</sup> and Rosenow<sup>23</sup> do not record any experiences with healed cases. Leyden believed that it was possible for "ulcerative" endocarditis to heal. He evidently had instances of subacute bacterial endocarditis among the cases he studied, but none with healed lesions.

<sup>18</sup> AMER. JOUR. MED. SCI., 1910, cxi, 516.

<sup>19</sup> Trans. Assoc. Amer. Phys., 1902, xvii, 48.

<sup>20</sup> Berlin. klin. Woch., 1899, p. 609, 644; Deutsch. med. Woch., 1902, p. 369, 395.

<sup>21</sup> Zeitschr. f. klin. Med., iv, p. 321.

<sup>22</sup> Loc. cit.

<sup>23</sup> Jour. Infect. Dis., 1909, vi, 249.

Harbitz,<sup>24</sup> in the report of his admirable investigations on endocarditis, discusses lesions that he found in 10 cases that he believes were related to "chronic infectious endocarditis," and in which the lesions were in a healing stage.<sup>25</sup> He says that he did not succeed in obtaining bacteria in these lesions, but the anatomical picture, "the extension to the walls of the auricle and ventricle, the excrescences on corresponding parts of two adjacent flaps, the tearing of chordæ tendineæ," etc., was quite characteristic. These cases ran a long course, at times associated with subacute nephritis. In one case of this group in which the cultures at the autopsy were sterile, Peter Holst obtained two weeks before death a "white staphylococcus" in the blood. In a few cases indistinct groups of organisms were found in sections and smears made from vegetations, and the cultures were negative. These observations of Harbitz are the most definite hitherto recorded.

Bartel<sup>26</sup> made a study of 22 hearts from cases of endocarditis to determine whether "ulcerative" endocarditis is capable of healing and how often it occurs. His Cases IV and VII resemble much some of the cases I have described. He discusses the possibility of relapses of infection due to bacteria lying dormant in healing or healed lesions, a subject to which I have alluded in an earlier publication,<sup>27</sup> and which is worthy of further study.

Lenhartz<sup>28</sup> states that none of his cases recovered. One case that left the hospital after the fever had disappeared, and the blood was free from bacteria, died ten months later of cardiac insufficiency. Horder<sup>29</sup> saw only one recovery in 150 cases of endocarditis due to all kinds of bacteria. The patient was a boy, aged fifteen years, who had fever for seven weeks. He eventually lost all evidences of cardiac disease. This observation loses in value because no blood cultures were made.

Latham and Hunt<sup>30</sup> describe the case of a man who was under observation from August 24, 1909, to November, 1910. They obtained a coccus from the blood, which may very well correspond to the endocarditis coccus, seven times between October and July. There was irregular fever and repeated embolisms. From April on there was gradual improvement. When the patient was seen in November, 1910, the temperature had been normal or subnormal for several months, the pulse rate was 60, and the heart was regular. The mitral systolic and aortic diastolic murmurs persisted. The last three blood cultures were negative. The authors make a note that the polynuclear percentage dropped

<sup>24</sup> Loc. cit.

<sup>25</sup> I am indebted to Dr. Baehr for drawing my attention to these 10 cases described by Harbitz.

<sup>26</sup> *Wien. klin. Woch.*, 1901, p. 1004.

<sup>27</sup> Libman, *Johns Hopkins Hosp. Bull.*, 1906, xvii, 223.

<sup>28</sup> *Die septischen Erkrankungen*, Wien, 1904, p. 434.

<sup>29</sup> *Quart. Jour. Med.*, ii, 289.

<sup>30</sup> *Proc. Royal Soc. Med., Clin. Sec.*, November 11, 1910, p. 14.

from 74 to 54 in the course of the case. I have a number of times seen lymphocytic increase in subacute bacterial endocarditis, in cases with and without bacteria.

They ascribe the recovery to the use of an autogenous vaccine administered by the mouth. As one so often sees spontaneous disappearance of the bacteria, this case may very well have become bacteria-free without the use of the vaccine. Vaccines have been used by many competent observers in these cases without any beneficial effect.

Emerson and Harrison<sup>31</sup> describe a case supposed to be one of the group under discussion, but it does not seem to me to be a case of subacute bacterial endocarditis.

Schottmüller,<sup>32</sup> in 1910, described 5 cases of subacute bacterial endocarditis ("endocarditis lenta"), and stated that 1 was still under observation and was doing well. The other 4 died. He has not reported since that time on the case that he believed was recovering.<sup>33</sup>

Jochmann<sup>34</sup> has recently reported 7 cases of the disease, 2 of which recovered; 3 of the cases were treated with an autogenous vaccine and with a serum produced by immunizing animals with cultures of the "*Streptococcus viridans*." Two of the patients so treated died. So that 1 case recovered on the use of specific treatment and 1 without it. It is to be hoped that the subsequent course of these 2 cases will be reported.

Some time ago I came across a reference to a case mentioned by Reiche, of Hamburg, at a meeting. He had a case of subacute bacterial endocarditis of the aortic valve in which the blood cultures became negative after they had shown cocci a number of times. The patient died of an embolic aneurysm of an intrahepatic branch of the hepatic artery which had ruptured into the liver substance and caused a fatal hemorrhage into the peritoneal cavity. The endocardial lesions, Reiche stated, were found healed. It is unfortunate that no further data are given as to bacteriological studies of the involved valve, and no accurate description of its appearance.

It will be noted that the observations on the healing of subacute bacterial endocarditis are rather few in number. From the pathological standpoint those of Harbitz are the most illuminating. From the standpoint of healing in a clinical sense the observations of Latham and Hunt and Reiche and Jochmann are important. It is essential that writers who in future report such cases give subsequent reports on the condition of the patients, with reference to the clinical points I have discussed in the body of this paper.

<sup>31</sup> Jour. Royal Army Med. Corps, 1910, xv, 588.

<sup>32</sup> Münch. med. Woch., 1910, p. 880.

<sup>33</sup> July 31, 1912. Since this paper was written, I have heard from Professor Schottmüller that this case has succumbed.

<sup>34</sup> Berlin. klin. Woch., 1912, p. 436.

It seems remarkable that the cases that have spontaneously become bacteria-free have hitherto escaped detection.

I believe I have brought forward sufficient evidence to prove that subacute bacterial endocarditis is a disease in which healing can occur from the bacteriological, pathological, and clinical standpoints, although the evidence of complete recovery from the clinical side is still very meagre.

It is a pleasant duty for me to express my gratitude to Drs. Rudisch, Meyer, Brill, and Manges, the visiting physicians to Mount Sinai Hospital, for their kindness during many years in permitting me to make studies on their cases. The clinical data are mainly derived from the cases in the service of Dr. Rudisch and from cases which a number of physicians permitted me to observe in their practice. I wish to add that it would not have been possible to complete the bacteriological and pathological studies as far as they have been carried without the enthusiastic assistance of the various members of the laboratory staff for the last ten years.

## GLOMERULAR LESIONS OF SUBACUTE BACTERIAL ENDOCARDITIS.<sup>1</sup>

BY GEORGE BAEHR, M.D.,

ASSISTANT IN PATHOLOGY, MOUNT SINAI HOSPITAL, NEW YORK.

IN the kidneys of nearly all individuals dying during the course of subacute bacterial endocarditis there exists a pathological lesion which affects one or more loops of a variable proportion of the glomeruli.<sup>2</sup>

The first to draw attention to this lesion and to connect it with infections of the endocardium by the endocarditis coccus (*Streptococcus viridans*) was Loehlein. In March, 1910, he reported 8 cases of this condition, in all of which loops of some of the glomeruli showed the lesions. Three of these showed organisms in blood cultures taken during life, and in one of these, organisms were cultivated from vegetations post mortem. In one case the lumen of an artery entering an infarcted area was occluded by an embolus which contained numbers of cocci.

Before proceeding to a consideration of the glomerular lesions it is necessary to understand a few of the cultural characteristics of the endocarditis coccus in order to be able to appreciate the mechanism by which the kidney lesions are produced. On the

<sup>1</sup> Read by invitation at the meeting of the Association of American Physicians, May 15, 1912.

<sup>2</sup> Baehr, Jour. Exp. Med., xv, 330.

surface of agar, its growth is exceedingly dry and sometimes difficult to remove. When an attempt is made to emulsify this growth in normal salt solution, the bacteria show a very marked tendency to hang together in small firm clumps which usually cannot be broken up even by very vigorous shaking.

Smears made from pieces of vegetations in these cases when squeezed between slides and stained by Gram's method, usually show the presence of the typical cocci in numbers such as are seen only in smears made from pure cultures. It is quite conceivable, therefore, that large numbers of these clumps are constantly being washed off the vegetations by the blood current, and being just small enough to pass the vasa afferentia in the kidney, become lodged in the capillary loops of the glomeruli.

In the kidneys of individuals dying during the active bacterial stage of the disease there are seen, as a rule, all stages of the glomerular lesions. The number of involved loops of a glomerular tuft varies in the different diseased Malpighian bodies. Furthermore, there is a great variation in the relative number of glomeruli involved in different parts of the kidneys. The uninvolved glomeruli and the uninvolved loops of involved glomeruli show no changes.

The very earliest stage of the process appears to consist of a swelling of the glomerular epithelium in the involved loops. This may be situated at any portion of the glomerular tuft. If the lesion is large, a segment of the glomerulus, or even the entire Malpighian body may be involved by the process. At first the outlines of the swollen epithelial cells in the diseased segment can be made out. Subsequently they are lost and the entire structure is fused into a homogeneous, finely granular material. In this mass some of the nuclei are fading or undergoing karyorrhexis, although a few may still remain fairly well preserved.

If the deep staining, finely granular mass is situated at the periphery of the glomerulus, the epithelium of the visceral layer of Bowman's capsule over the involved part is usually found to be swollen, proliferating, and desquamating into the capsular space. When the mass with its overlying epithelium comes into contact with the parietal layer of Bowman's capsule, the latter then probably also takes a share in the desquamation, and perhaps in the proliferation.

Eventually this epithelium undergoes necrosis, as did the previously swollen epithelium of the involved loops of the glomerulus. It also becomes part of the homogeneous, finely granular mass which now fuses with the parietal layer of Bowman's capsule. At this stage, the mass may become flattened out over the area of fusion with Bowman's capsule in a crescentic fashion.

The homogeneous cellular material is seen to be traversed by a very delicate network. Eventually the entire mass becomes

thoroughly organized. At the same time there occurs active growth of the epithelial cells of the adjacent intact portions of the parietal layer of Bowman's capsule. They advance over the inner aspect of the necrotic mass which by this time has usually separated somewhat from the rest of the glomerulus. Eventually the entire lateral surfaces of the mass are covered by this invading epithelium.

The healed stage of the lesion presents the following picture: A hyaline mass having roughly the shape of a truncated pyramid; its base fused with the adjacent interstitial tissue; its mesial aspect adherent to the remainder of the glomerulus; its sides clothed by a reflection from the adjacent epithelium of Bowman's capsule.

When the entire glomerulus is involved, the peripheral portion may be seen to be replaced by concentric fibrils of connective tissue, whereas the central portion still consists of a homogeneous material. In the same section, however, examples of even later stages are frequently seen, the glomerulus being entirely replaced by a mass of hyaline fibrous tissue.

Practically every stage of the process described above is to be seen in nearly every microscopic section of the kidney cortex from most of the cases, and this association of the various stages is an important part of the pathological picture.

The typical lesions were found in 23 of the 25 cases due to the endocarditis coccus. In 2 cases, 1 of which was due to the influenza bacillus and 1 due to the gonococcus, the lesions were not found. The percentage of glomeruli involved varied from 2 to 75 per cent. in various cases.

In sections of 5 cases in which portions of the kidneys were fixed in alcohol, Gram-Weigert stains demonstrated bacterial emboli in the capillaries of the glomeruli. In 2 cases they were easily found; in the other 3, they were only discovered after prolonged search.

The changes that occur in the tubules and interstitium and in the end may lead to a picture identical with that of the secondary contracted kidney are discussed in the paper already referred to. In the same paper will be found a description of the atypical lesions which were found in 2 cases and which closely resembled the lesions found in subacute glomerular nephritis.

In 54 cases of acute endocarditis due to the ordinary pathogenic bacteria, none of the glomerular lesions were found in any case. In the cases which Dr. Libman has described as being instances of a healed or bacteria-free stage of subacute bacterial endocarditis; the characteristic lesions were found every time, only the healed stage of the lesion being present. In these cases the lesions were less abundant than in cases in which the endocarditis coccus had been found during life or after death.

## THE RELATION OF HYPERTENSION TO URINARY EXCRETION.

BY CHARLES H. LAWRENCE, JR., M.D.,

ASSISTANT VISITING PHYSICIAN, MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

(From the Henry P. Walcott Fellowship, Harvard Medical School, and the Massachusetts General Hospital.)

WHEN Bright<sup>1</sup> described the condition now known as cardio-renal disease he advanced the following theory to explain the cardiac hypertrophy and increased tension of the pulse which he recognized as characteristic of the condition. There occurred, he thought, a change in the quality of the blood by virtue of which it acted as a stimulus to the heart, causing it to beat more forcibly, and thus hypertrophy, with resulting increase in the force of the pulse. Further, he considered it possible that the blood might act upon the capillaries, causing them to contract and thus demand greater work from the heart in forcing the blood through them.

Opposed to Bright's theory is that of Traube,<sup>2</sup> which is purely mechanical. According to this theory the destruction of vessels in the damaged kidneys causes (1) a diminished rate of outflow from the aorta, and (2) an increased resistance to the outflow from the renal arteries. Then follows permanent high tension and cardiac hypertrophy.

Cohnheim's<sup>3</sup> theory in some measure combines the ideas advanced by Bright and Traube. He states that the caliber of the renal vessels, great and small, depends upon the amount of urinary constituents (urea, water, etc.) present in the circulating blood. If these become increased a contraction of the vessels takes place. Under these conditions, if the amount of blood passing through the kidneys is to remain unchanged a rise in pressure, compensatory in nature, must follow.

Cohnheim's theory has been most generally accepted, and the present belief concerning the nature of hypertension has for its fundamental concept the compensatory role of increased blood pressure. The influence of Bright remains in the belief that in nephritis the blood does contain some toxic material of an as yet unknown nature.<sup>4</sup>

It is toward the elimination of this unknown toxin that treatment is principally directed, and little attention is paid, from a therapeutic standpoint, to the arterial tension. The diet, low in proteid, the hot air baths, the vigorous catharsis, and in selected cases

<sup>1</sup> Quoted by Senator, *Zeitschr. f. klin. Med.*, 1911, lxxii, 189.

<sup>2</sup> *Allgemeine Pathologie*, 1882, ii, 357.

<sup>3</sup> *Quarterly Jour. Med.*, 1909, ii, 231.

<sup>4</sup> *Ibid.*

venesection, all aim toward the elimination of toxic material. Restriction of fluid intake has for its purpose removal of edema by reabsorption and elimination through the bowel or skin. Cardiac decompensation is combated with digitalis.

There can be no doubt that these measures do cause an increased general elimination from the body (though the amount of toxin removed must remain an open question until it is identified). There is equally little doubt that with the exception of digitalis they cause a fall in blood pressure. In a previous paper the writer has tabulated observations as to the effect of most of these measures upon systolic and diastolic pressure. The results show that with the exception of the administration of digitalis all the measures mentioned above cause a diminished arterial tension in the majority of cases. It has long been held that digitalis causes an increase in blood pressure, but in a recent article Cushney<sup>5</sup> states that he was surprised to find that the increased tension caused by digitalis in animals did not obtain in a large series of human patients whom he had observed.

Here then exists a conflict. It is generally believed that high blood pressure is a protective reaction in renal disease. The treatment of such disease, while principally directed toward the elimination of toxic material from the body, has a depressing effect on blood pressure. Are the good results ascribed to the treatment entirely due to its eliminative effect, and do they occur in spite of its depressing action upon the protective hypertension? Or is the lowering of the abnormally high tension responsible for some of the improvement noted? In short, is hypertension in nephritis essentially protective, or is it merely an evidence of the action of a circulating toxin upon the vessels?

According to Conheim it is protective in nature. Its purpose is to force the blood in undiminished amount through kidneys which offer increased resistance to its passage. Experimental evidence, however, raises objections to this theory.

Senator<sup>6</sup> has shown that ligature of the renal artery or extirpation of the kidney does not cause a rise in arterial pressure.

Objection has been raised to this maneuver by Katsenstein,<sup>7</sup> who states that complete ligation of the renal artery does not have the same effect as a marked but incomplete narrowing of its lumen. In his experiments on dogs he found that the latter operation always caused a rise in arterial pressure, never amounting to more than 10 mm. of mercury. Senator, however, was unable to confirm these results and found that there was no greater rise in pressure than when the femoral artery was similarly treated.

Under Senator's direction the following experiments were carried out. Animals were narcotized with urethran to eliminate sensory

<sup>5</sup> AMER. JOUR. MED. SCI., 1911, clxi, 469.

<sup>6</sup> Zeitschr. f. klin. Med., 1911, lxxii, 189.

<sup>7</sup> Virchow's Archiv, 1905, clxxxii, 327.



stimuli as a factor in raising the pressure. Paraffin was then injected into the kidneys, completely "infarcting" those organs, as autopsy later showed. "The blood pressure measured in the carotid artery showed no rise, even at the end of an hour." From these experiments Senator concludes: "In so far as one can argue from cats to man I believe it conclusively shown that through damaging the blood flow to the kidney parenchyma, with unhindered flow to the renal artery, the pressure in the aortic system is not raised."

The effect of high pressure upon the volume of blood passing through the kidneys has been studied by Burton-Opitz, and Lucas.<sup>8</sup> They measured the volume of blood flowing through the kidneys of animals in a unit of time during which the pressure in the arterial system was normal. The general pressure was then raised, and the volume flow through the kidney again recorded for a similar length of time. The observers found that in "by far the largest number" of experiments there was no increase in the flow of blood through the kidney, "even at a time when the very pronounced rises in arterial pressure had fully developed." In a number of experiments they found that the increased pressure was accompanied by a diminution in the volume of blood flowing through the kidney.

Schlayer and Hedinger<sup>9</sup> carried out a series of similar experiments. They, however, measured changes in the kidney volume instead of changes in the blood flow. They found that a rise in blood pressure due to sensory stimulation or to administration of adrenalin was accompanied by a diminution in kidney volume, while caffeine caused a dilatation of the renal vessels and a resultant diuresis. They further found that in toxic nephritis there was a loss of power of dilatation of the renal vessels and a loss of diuretic action from the above drug. The loss of contractile power of the renal vessels was slight or none.

Von Passler and Heinecke<sup>10</sup> removed successive small amounts of tissue from the kidneys of dogs and studied the effects of the loss of substance upon blood pressure and upon elimination of urine. They conclude that the polyuria observed in nephritis is independent of blood pressure, but bears a direct relation to loss of kidney substance.

Fischer<sup>11</sup> in a research upon causes of edema performed the following experiments: A filter of colloid material was inserted in an artificial circulation scheme through which fluid was pumped under varying but known degrees of pressure. The colloid substance of the filter was acidulated to varying but definite amounts. The amount of fluid passing through the filter and that returned

<sup>8</sup> Jour. Exp. Med., 1911, xiii, 308.

<sup>9</sup> Deut. Arch. f. klin. Med., 1907, xc, 1.

<sup>10</sup> Verhand. der Deutsch. pathol. Gesell., 1905, ix.

<sup>11</sup> Edema, 1911.

by it in a unit of time were determined. The results showed that the acidity of the filter was the paramount factor in determining the amount of fluid retained by it, and that any effect obtained by increasing the pressure behind the filter could be vitiated by increasing the acidity of the colloid material. From these results it is suggested that the affinity of cells for water, determined by their chemical composition, controls the amount of urine excreted, while the pressure behind the kidney is of secondary importance.

To sum up: Experiments on animals show that (1) high blood pressure is not caused by increased resistance to the flow of blood through the kidney; (2) that it does not cause increased flow through those organs, and (3) that it is not the cause of the polyuria so often seen in that class of kidney disease, commonly accompanied by hypertension.

Opposed to the conclusions drawn from experiments on animals stands the opinion, often expressed by clinical observers, that hypertension is nature's way of protecting the organism against the deleterious effects of damage to the kidney. This opinion is derived from the observation of large numbers of patients. Moreover, it has often been observed that when such patients suffer acute exacerbations the systolic pressure is less high than during the periods of comparatively good health. In the experience of many careful observers an attempt to lower the blood pressure by the use of vasodilators causes headache, dyspnea, and other symptoms characteristic of uremia. For these reasons it is believed by many that hypertension existing for years tends to protect the organism from the result of diminished renal activity, and that when the heart can no longer maintain the pressure at a sufficient height the patient suffers from uremia.

Scattered through the literature are reports that disagree with this theory. Thus Gibson<sup>12</sup> states, "If there is considerable increase (in pressure) in acute nephritis the prognosis is less favorable than when there is no rise at all," and in the same article, "A rise in pressure above what has been found to be the normal for the case is very commonly the herald of uremia."

Miller<sup>13</sup> reports the following case: A patient entered the hospital having uremic convulsions; blood pressure, 200 mm.; twenty-four hour amount of urine, 600 c.c. Under treatment the pressure fell to 130 mm., the convulsions disappeared, and the twenty-four hour amount of urine rose to 1700 c.c. There was no change in the amount of fluid ingested.

Kinnicutt<sup>14</sup> states, "The power of nitroglycerin to control or relieve many of the paroxysmal disturbances of the nervous system included under the general term uremia was more marked than that of opium or chloral."

<sup>12</sup> Edinburgh Med. Jour., 1911, vi, 197.

<sup>13</sup> Jour. Amer. Med. Assoc., 1910, liv, 1666.

<sup>14</sup> Med. Record, 1886, xxix, 255.

Dana<sup>15</sup> cites 6 cases of renal disease and 5 normal cases in which administration of nitroglycerin was followed by diuresis.

Elliott<sup>16</sup> sums up the situation as follows: "As a matter of fact there is no certain correspondence between the amount of urine excreted and the degree of blood pressure. The administration of a nitrite to lower blood pressure will as often be attended by an increase as by a fall in the amount of urine.

A. Loeb<sup>17</sup> holds the same theory, but on the basis of 3 cases in which the administration of nitroglycerin was followed by a fall in the amount of urine decides that lowering the pressure has a deleterious effect upon renal activity.

The evidence obtained by careful observation of cases is most valuable. From it must be made the final decision as to the validity of any theory founded upon experiments on animals. Many conditions occurring in man cannot be exactly reproduced in animals. Among them is cardiorenal disease. Therefore the results of animal experimentation are less convincing in this condition than in many others. More important and convincing are observations carried out on human beings under circumstances artificially produced and therefore accurately estimated.

Among such observations the most extensive are those of Erlanger and Hooker,<sup>18</sup> made with the aid of an instrument devised by Erlanger. They made numerous observations on the relation of circulatory conditions to renal activity. The subjects were two medical students: one a normal individual, and one suffering from orthostatic albuminuria. On the basis of their experiments they conclude that no relation can be discovered between the output of urine or albumin and the blood pressure, either systolic or diastolic. They conclude that the amount of urine excreted by the individuals studied varied directly as the pulse pressure, that is, the difference between systolic pressure and diastolic pressure. Hooker<sup>19</sup> working alone later obtained similar results. His experiments were performed upon isolated kidneys, but his results are similar to those reached by Erlanger and himself.

The conclusion of these writers based upon a large number of careful observations are at variance with the results of clinical observation. The individuals observed, however, did not have abnormally high blood pressure. Therefore, it is unsafe to conclude from them that hypertension does not increase the amount of urine excreted by nephritic kidneys. The results do suggest such a possibility, however, and in conjunction with the work of Fischer, already cited, form a basis for an hypothesis, that hypertension in nephritis does not aid urinary excretion. If this be the case,

<sup>15</sup> Med. Record, 1886, xxix, 255.

<sup>16</sup> AMER. JOUR. MED. SCI., 1910, cxi, 6.

<sup>17</sup> Deutsch. Arch. f. klin. Med., 1905, lxxiv, 579.

<sup>18</sup> Johns Hopkins Hosp. Rep., 1904, xii, 145.

<sup>19</sup> Amer. Jour. Phys., 1910, xxxvii, 24.

the idea that it is a protective reaction loses much of its support, and the theory that it represents merely vascular spasm becomes strengthened.

One important piece of evidence is lacking—that obtained by accurate observation of human beings suffering from nephritis and hypertension under conditions which could be varied at the will of the observer, and thus more accurately estimated than is possible under the usual conditions.

It was in the hope of supplying some part of this evidence that the work reported here was undertaken. Its purpose was to ascertain whether a large number of observations would show any definite relation between the excretion of urine and the changes in systolic and diastolic blood pressure or pulse pressure occurring in individuals suffering with chronic nephritis. Observations were made upon 20 patients, all of whom had polyuria, albuminuria, cardiac hypertrophy, and an average systolic pressure of over 180 mm. of mercury. During the entire period of observation the daily amount of liquid intake and urinary output was measured and recorded. The diet was not materially changed during the observations. As far as possible drugs were administered one at a time, and the effect of each studied before another was added. No results were recorded which were obtained before blood pressure, urinary excretion, and elimination by the intestine had recovered from the wide variations seen during the first days of a patient's stay in the hospital and had approximated a daily level. Blood pressures were estimated with a Faught mercury manometer equipped with a cuff 12 cm. wide.

Systolic pressure was estimated at the point at which the first returning pulse beat was palpable after all pulsation had been obliterated. Diastolic pressure was estimated by the auscultatory method.<sup>20</sup> The estimations were made twice daily: in the middle of the morning and the middle of the afternoon, at least two hours after meals. Three readings were made at each sitting and the average recorded as the pressure at that time. Patients were always in the prone or semiprone position. Observations were always made on the same arm in each individual. The patient was quiet for at least one-half hour before the observation.

The urinary output for each day was likewise recorded. Any change therein which was accompanied or immediately preceded by an equal change in liquid intake was discarded from the records. The variations in the amount of fluid taken in twenty-four hours by any patient were slight, the individuals usually taking their entire allowance.

The pulse rate was recorded four times daily, and all observations which showed a change in rate of over eight beats per minute were

<sup>20</sup> Deutsch. Arch. f. klin. Med., 1908, xciv, 441.

excluded from the tables. Changes in pulse rate can therefore be fairly excluded from the causes of fluctuation in urinary output.

All observations made during a period in which the patient's temperature was more than one degree above the normal were also discarded from the final results. As it has been shown an increase of temperature causes an increased rapidity of circulation. (Hewlett<sup>21</sup>).

Six hundred and twenty-seven observations upon changes in blood pressure and coincident changes in urinary output were recorded. Four hundred and twenty-two of these contained one or more of the sources of possible error mentioned above. These were excluded from the results, which are based upon 205 observations.

The 205 observations are divided into six groups. Group I contains all the observations showing a rise in systolic pressure; Group II all those showing a fall. In Groups III and IV are placed similar changes in diastolic pressure. Groups V and VI contain those observations showing respectively increased and decreased pulse pressures. Each change in pressure is accompanied by the coincident change in urinary output.

From the results thus obtained there appears no definite relation between changes in systolic or diastolic pressure *per se* and changes in urinary excretion. There was a slightly larger number of instances in which a fall in pressure was accompanied by increased urinary output, but the difference was never greater than 20 per cent.

When, however, the cases of increased pulse pressure are analyzed, interesting results appear. It was found that whenever increased pulse pressure occurred in connection with a fall in systolic pressure the urinary output was increased. When, however, increased pulse pressure was due to a systolic rise, increase in urinary output occurred only in half the cases. Thus it appears that increased pulse pressure if due to a systolic rise may or may not be accompanied by a diuresis, but is always so accompanied if it be due to a systolic and diastolic fall. In other words, an increase in the caliber of the vascular system seems to be more efficient in promoting diuresis than does increased pressure in the aorta and its great branches.

The chief objection to the evidence cited above is that it lacks precision. It was, of course, impossible to estimate the pressure continuously during the twenty-four hours. For this reason there is a potential source of error in accepting the daily average pressure as that at which the entire twenty-four hour amount of urine was excreted.

It seemed advisable, therefore, to control the observations cited above by a series extending over a shorter time, during which a

more accurate estimate of conditions would be possible. For this purpose the method of studying the functional activity of the kidneys devised by Rowntree and Gerraghty<sup>22</sup> was employed. The test was performed in each case by Dr. E. L. Young, Jr. Dr. Young, whom I wish to thank for his help, also estimated the amount of phenosulphonephthalein excreted and measured the amounts of urine obtained. Thus the tests were carried out by one experienced in the technique, and the personal element was eliminated from the results, since neither observer knew the results of the other's work until the test was finished. By the test, the amount of urine and of test dyestuff excreted during one hour was determined. During this time systolic and diastolic pressure and pulse rate were determined at five-minute intervals. Two tests were performed on each patient: one while the daily pressure was at its constant high level, and one while it was lowered by administration of nitrites.

Eighteen patients were so tested. The results of the tests are placed in three groups as follows:

Group I, 3 cases, which showed a lessened urinary output when the blood pressure was lowered by nitrites. The patients upon whom these observations were made were in the last stages of cardiorenal disease, and their urinary excretion was not increased by any of the numerous methods used.

Group II, 12 cases, which showed an increased elimination of urine, phenosulphonephthalein, and urinary solids (as estimated by the specific gravity) during the period in which the systolic pressure was lowered by the administration of nitrites. The total nitrogen excretion was estimated by the Kjehldal method in 6 of these cases. In all there was increased nitrogen elimination during the period of lowered pressure.

Group III, 3 cases which gave results similar to those in Group II. The changes observed were, however, so small that they might have been due to technical errors. These cases are therefore not considered in the results.

In the 12 cases of increased elimination there was considerable variation in the diuresis obtained, the most marked change occurred in an arteriosclerotic patient whose average daily systolic pressure was 230 mm. of mercury. At that pressure he excreted in one hour 90 c.c. of urine containing 11.8 per cent. of phenosulphonephthalein. With an average systolic pressure of 190 mm. (the fall being due to sodium nitrite) he excreted 485 c.c. of urine and 50 per cent. of phenosulphonephthalein.

Continuous administration of a vasodilator in the cases cited above showed that a tolerance was soon developed by the patient. In from thirty-six to forty-eight hours the pressure returned to its

original level, and as it rose the amount of urine fell, each reaching its original figure at about the same time. A further administration of the nitrites caused no change in pressure and no diuresis. In cases in which the nitrites caused no fall in blood pressure there was no diuresis. In 3 cases in which venesection was performed the fall in pressure and increase in pulse pressure was immediately followed by a rise in urinary output. It seems fair to assume, therefore, that the urinary increase noted in connection with a fall in systolic pressure was due to that fall, since the latter was the only variable factor detected.

These results differ slightly from those obtained by observation of the changes already discussed. In the former the changes in pressure were not the direct result of any change in treatment, and diuresis was due apparently to the increased amplitude of pulse pressure *per se*. In the cases treated with nitrites, however, the pulse pressure was diminished slightly. This diminution was, however, probably compensated by the increased output of the heart which occurs, according to Cameron,<sup>23</sup> Hewlett,<sup>24</sup> and Hirschfelder<sup>25</sup> when nitrites are administered.

The final deductions to be made from these observations may be set down as follows:

1. No definite relation could be established between changes in systolic or diastolic pressure *per se* and variations in urinary output.

2. There appeared to be a definite relation between changes in pulse pressure and urinary output, for whenever the former increased in the presence of a falling systolic pressure there occurred a diuresis.

3. The administration of a nitrite which has been shown to increase the volume output of the heart caused a diuresis even though pulse pressure was somewhat diminished by the systolic fall. In all instances in which a rise in urinary output was noted there was one characteristic change in the pressures noted. That change was an approach to what Gibson<sup>26</sup> calls the normal circulatory coefficient. Under normal conditions the ratio of diastolic pressure to systolic is 2 to 3; the ratio of pulse pressure to systolic pressure, 1 to 3. Under conditions of hypertension this ratio is destroyed. Whenever in the observations here cited the several pressures approached their normal ratios there was a rise in urinary excretion.

These facts are not in accord with the generally accepted theory of the relation of blood pressure to urinary secretion. As quoted by Osler,<sup>27</sup> that theory states that "the activity of the circulation through the kidneys at any moment—in other words the state of

<sup>23</sup> Interstate Med. Jour., 1911, xviii, 595.

<sup>25</sup> Interstate Med. Jour., 1911, xviii, 556.

<sup>27</sup> Practice of Medicine, 697.

<sup>24</sup> Loc. cit.

<sup>26</sup> Loc. cit.

the small arteries as regards the contraction or dilatation depends not upon the need of those organs for blood, but solely upon the amount of material for urinary secretion that the circulating fluid happens to contain. When parts of the kidney have undergone atrophy the blood flow through the part that remains must, *cæteris paribus*, be as great as to the whole of the organ if they had been intact. But in order that such a quantity of blood should pass through the restricted capillary area, now open to it, an excessive pressure must obviously be necessary."

Thus the theory, yet the evidence cited has shown: (1) That excessive pressure not only does not cause increased flow through the kidneys, but may in extreme cases diminish it. (2) That destruction of large amounts of kidney substance or obliteration of the capillary circulation of those organs does not bring about an increase in blood pressure. (3) That a diminution of the hypertension of renal disease may cause increased function of the kidney.

There can be no conciliation between the theory as stated and the facts as experiment and observation bring them to light. From the former it appears that renal function is dependent upon pressure at which the blood passes through the kidneys. From the latter it appears that renal function is dependent upon the amount of blood passing through the kidney in a unit of time and that the pressure is unimportant. It is therefore necessary either to controvert the results here cited or to propound another theory which shall be in accord with the facts as they now stand.

Such a theory has recently been evolved by Fischer.<sup>28</sup> Briefly stated it is as follows: The retention of fluid by living cells is dependent not upon mechanical conditions, but upon the affinity of those cells for fluid. This affinity is increased when the colloids of the cells become more acid than normal. The colloids of the cells become abnormally acid under any conditions that interfere with the proper oxygenation of the tissues. Such a condition is found in nephritis.

The facts here cited may be easily explained on the basis of Fischer's theory, for according to it the rate of circulation would be the controlling factor in determining urinary output, and not the pressure under which the blood flowed. Thus an increase or decrease in systolic or diastolic pressure might or might not be associated with an increased oxygenation of the kidney. If it were urinary output would increase, if not, it would remain stationary or fall. This is exactly what does take place according to the evidence here cited. The explanation of the diuresis associated with increased pulse pressure is simple upon the basis of Fischer's theory, for if the pulse pressure be increased the efficiency of the circulation is enhanced, and an increased supply of oxygen is

<sup>28</sup> Fischer, Nephritis, 1912.



therefore carried to every organ. Its acidity is therefore diminished, its affinity for fluid grows less, and diuresis results. In a similar way the diuresis obtained with a vasodilator may be explained, though in that case the increased oxygen supply is due in part to the action of the drug directly upon the heart.

Here then is a theory which appears to have no quarrel with the facts. It is based upon evidence obtained from animal experimentation and from the use of artificial circulation schemes, and has been confirmed in a few instances by observations on man. Observations upon human beings intended to establish the application of Fischer's theory to conditions as they are found in chronic nephritis offer an interesting field for clinical research, and evidence thus obtained will be necessary to make clear the relation of circulatory conditions to urinary excretion.

I wish to express my thanks to Dr. F. C. Shattuck for making this work possible and for encouragement at all times. My grateful acknowledgement is also due to all the members of the hospital staff who rendered me aid whenever called upon.

TABLE I.—Changes in Systolic Pressure.

	Number.	Per cent.
Changes in systolic pressure recorded . . . . .	105	
Increased pressure recorded . . . . .	48	45.7
Increased pressure associated with rise in urinary output . . . . .	20	41.6
Increased pressure associated with fall in urinary output . . . . .	28	58.4
Decreased pressures recorded . . . . .	57	54.3
Decreased pressure associated with rise in urinary output . . . . .	33	57.9
Decreased pressure associated with fall in urinary output . . . . .	24	42.11

TABLE II.—Changes in Diastolic Pressure.

	Number.	Per cent.
Changes in diastolic pressure recorded . . . . .	100	
Increased pressures recorded . . . . .	52	52.0
Increased pressure associated with rise in urinary output . . . . .	19	36.5
Increased pressure associated with fall in urinary output . . . . .	33	63.5
Decreased pressures recorded . . . . .	48	48.0
Decreased pressure associated with rise in urinary output . . . . .	31	64.5
Decreased pressure associated with fall in urinary output . . . . .	17	35.5

TABLE III.—Changes in Pulse Pressure.

	Number.	Per cent.
Changes in pulse pressure recorded . . . . .	109	
Increased pulse pressure recorded . . . . .	56	51.3
Increased pulse pressure associated with rise in urinary output . . . . .	32	57.1
Increased pulse pressure associated with fall in urinary output . . . . .	24	42.9
Decreased pulse pressure recorded . . . . .	53	48.7
Decreased pulse pressure associated with rise in urinary output . . . . .	23	43.3
Decreased pulse pressure associated with fall in urinary output . . . . .	30	56.7
Increased pulse pressure associated with fall in systolic pressure . . . . .	32	
Instances associated with rise in urinary output . . . . .	32	100.0
Instances associated with fall in urinary output . . . . .	0	0

## THE BRAIN LESIONS PRODUCED BY ELECTRICITY AS OBSERVED AFTER LEGAL ELECTROCUTION.

BY EDWARD ANTHONY SPITZKA, M.D.,

DIRECTOR AND PROFESSOR OF GENERAL ANATOMY, THE DANIEL BAUGH INSTITUTE OF ANATOMY OF  
THE JEFFERSON MEDICAL COLLEGE,

AND

HENRY E. RADASCH, M.D.,

ASSISTANT PROFESSOR OF HISTOLOGY AND EMBRYOLOGY, JEFFERSON MEDICAL COLLEGE,  
PHILADELPHIA:

(From the Laboratories of the Daniel Baugh Institute of Anatomy.)

THE rapid growth in the employment of electricity in the industries and in general traffic and the concomitant increase in the annual lists of accidental injuries and deaths from industrial currents render it of interest to note what effects result in various parts of the human organism. The observations of one of the writers have been assembled in several papers and published during the last decade<sup>1</sup> and while mention is made of a peculiar type of brain lesions which has apparently not been observed as a resultant of any other mode of death, the present contribution is to give more explicit details, the result of investigations upon the brains of 5 criminals executed by electricity. We are particularly prompted to submit our observations because of the constancy of the appearance of those lesions.

The nature of the current employed in electrocutions is described in the papers cited.

*Technique.* The axial portion (pons-oblongata and midbrain) of 5 brains was subjected to careful histological examination after fixation in formalin, the immersion of the brain into the preservative usually occurring within fifteen minutes after death. Each brain stem was subsequently divided transversely into six to eight segments, dehydrated, cleared, and infiltrated with celloidin. Sections were then cut at 15 to 20 $\mu$  and stained, some with hematoxylin and eosin, some with Van Gieson's stain, and some with Weigert's myelin stain.

A general examination of the slides thus prepared revealed at all levels peculiar areas, varying in size and number. These areas, unlike anything ever seen before by the authors, are circular in outline, ranging in diameter from 25 to 300  $\mu$ . The most marked areas measure from 150 to 200 $\mu$ . They are seen to consist of two portions, a central rarified part and a peripheral condensed zone.

<sup>1</sup> Amer. Jour. Insanity, 1902; New York Daily Med. Jour., February 1, 1904; Med. Critic, August, 1903; Proc. Amer. Philos. Soc., xlvii (read April 23, 1908); Jour. Med. Soc., New Jersey, 1909; Philadelphia Electric Current News, April, 1911.

The most characteristic areas contain a bloodvessel (capillary or precapillary), surrounded by a delicate small-meshed reticulum representing the central four-fifths of the area. The fibrils of the reticulum are, in the main, radially directed, and nuclei are sometimes observed along this course. The peripheral zone surrounding the central portion in a ring-like manner appears to be condensed, staining more deeply than the surrounding unaffected tissue, and is sometimes seen to be composed of circularly arranged strata, which are usually free from nuclei.

The detailed study of each specimen resulted as follows:

CASE I.—J. B., executed at ——— prison, July 17, 1905. Two contacts, 1.07<sup>s</sup> and 0.05<sup>s</sup>; max., 1780 volts, 8 ampères.

SPINAL CORD, UPPER CERVICAL REGION. Here these areas are fairly large and numerous, but mainly unilateral. They are chiefly grouped in the ventral horn, and are scattered from there to the midperipheral area of the white substance.

AT HIGHER LEVELS. At higher levels the areas increase in number becoming quite plentiful in the interolivary white substance, among the central longitudinal fiber tracts, and in the formatio reticularis generally. The olivary gray and the various nuclei have not escaped; in fact, the lesions seem to have become grouped in and about the olivary body, while the peripheral fiber tracts have been largely spared.

PRE-OBLONGATA (PARS DORSALIS PONTIS). The ventral two-thirds of the area of the section (that is, just dorsad of the pons proper) is seen to be fairly riddled with lesions, while the dorsal one-third just ventrad of the ventricular floor contains but few areas. Where they exist they are more scattered than in the lower levels; as a rule, the areas are small, but well defined and characteristic. The largest are nearest to the mesal line.

At the level of the inferior quadrigemina the lesions are less numerous, but are of larger size, and are situated mainly in the longitudinal fiber tracts. Higher up at the level of the pregemina the sections are seen to be riddled in all parts of the field.

CASE II.—M. E., executed at ——— prison, April 10, 1905. Two contacts, 1.06<sup>s</sup> and 0.03<sup>s</sup>; 1750 volts, 9 ampères.

CERVICAL CORD. Many small areas are seen in the white substance, giving the section a cribriform appearance. The gray substance contained only a few lesions, 15 to 30 $\mu$  in diameter, but of a characteristic appearance.

POSTOBLONGATA. At the level of the pyramidal decussation the lesions are very numerous and a little larger than in the cervical cord. They are scattered diffusely in both gray and white substances, and are 25 to 40 $\mu$  in diameter. At this level the capillaries seem more involved, since the nuclei along the inner circumference of the outer zone seem to be those of the capillary endothelium.

At the level of the olive the areas are more numerous, larger



FIG. 1.—Section of middle of pons of J. B.

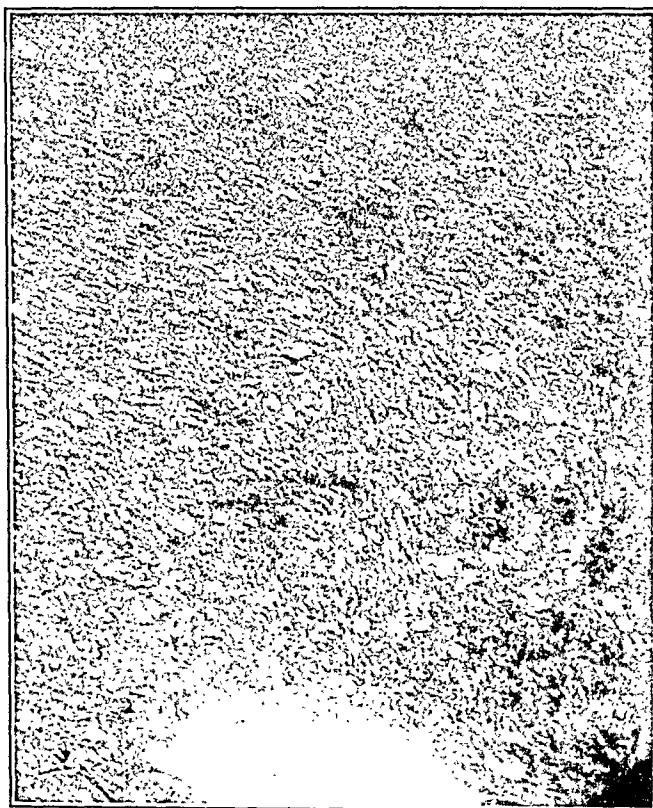


FIG. 2.—Section of brain stem of M. E., at level of inferior cerebellar peduncle.  $\times 80$ .

and more localized near the mesal plane (raphé), and involving mainly the longitudinal fiber tracts.

PREOBLONGATA. The lesions here are less numerous again, and are situated mainly in the dorsal part of the sections.

MIDBRAIN. In the midbrain sections the largest areas are near the mesal line and just ventrad of the central aqueduct gray. The smaller areas occupy the remainder of the sections. The longitudinal fiber tracts present a ragged appearance, as though they had been badly torn by some diffusely explosive or disruptive force. Occasionally there are seen ruptured myelin sheaths, which respond to Weigert's stain.

CASE III.—G. G., executed at ——— prison, February 25, 1907. Three contacts,  $1.04^s$ ,  $0.10^s$ ,  $0.07^s$ ; 1820 volts,  $9\frac{1}{2}$  ampères.

POSTOBLONGATA. In the region of the pyramidal decussation the lesions are, preponderatingly, unilaterally situated. They are located mainly in the gray substance, though a few are noted in the dorsal tracts. The myelin seems altered in some inexplicable way, for it does not respond well to the stain. Longitudinal sections of bloodvessels reveal the arrangement of these lesions as being perivascular, spherical expansions like beads along and about the vessel wall. (A structural peculiarity noted in this region was a duplication of the central canal.)

PREOBLONGATA. The areas here are small, but numerous mainly in the longitudinal fiber tracts, which exhibit a ragged appearance, while the transverse fiber tracts seem to be unaffected.

MIDBRAIN. At the level of the postgemina the ragged appearance of the longitudinal tracts is very marked as is also the distention of the vessels. At a higher level the lesions are less numerous and the ragged appearance of the white substance is less marked.

CASE IV.—A. S., executed at ——— prison, March 9, 1908. Four contacts,  $1.02^s$ ,  $0.05^s$ ,  $0.10^s$ ,  $0.05^s$ ; 1880 volts, 9 to 11 ampères.

Sections of the brain stem at various levels reveal the characteristic lesion, areas much the same as described in Case I. They are everywhere quite numerous, the more so and largest in the preoblongata.

CERVICAL CORD. Here the lesions are few in number, but distinctly marked.

CASE V.—G. W., executed at ——— prison, March 3, 1908. Two contacts,  $1.10^s$ ,  $0.06^s$ ; 1850 volts, 8 to 11 ampères.

Sections of this brain stem reveal the largest and most characteristic lesions and serve as the best examples for general study and illustration.

SPINAL CORD, CERVICAL PORTION. Sections of the upper part of the spinal cord show large areas situated chiefly in the white substance, and most numerous in the dorsal columns close to the gray substance. At the pyramidal decussation they are less numerous and smaller, and at higher levels diminish in number, with,

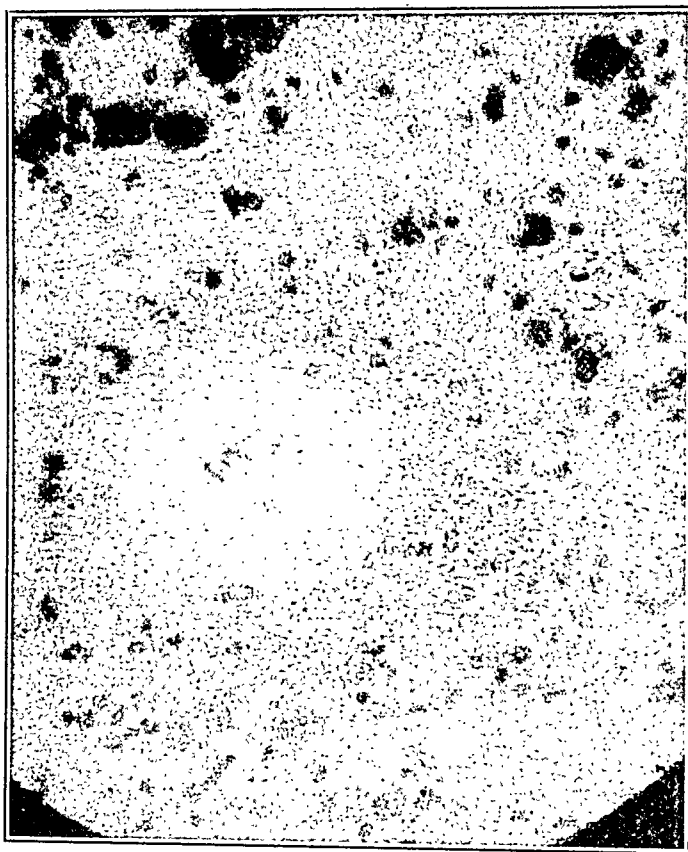


FIG. 3.—Section of pars dorsalis pontis of G. W.  $\times 420$ .

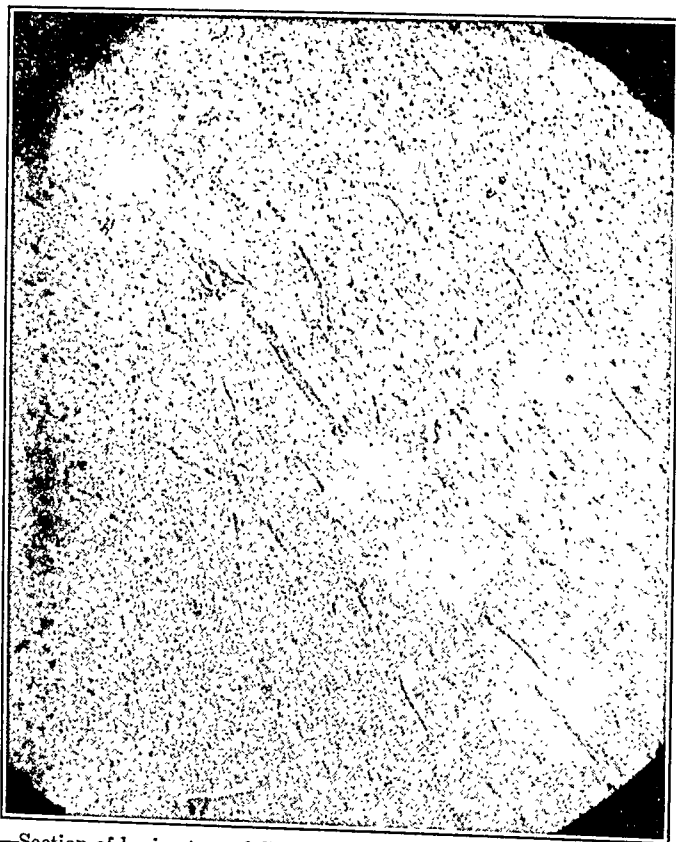


FIG. 4.—Section of brain stem of G. W., at junction of pons and oblongata.  $\times 110$ .

however, an increased proportion of areas containing bloodvessels. At the level of the caudal end of the olive these lesions are numerous and large, averaging 150 to 250 $\mu$  in diameter, while the white substance presents a ragged appearance. In the midolivary sections the lesions are still numerous and fairly large. Many vessels apparently show the effect of a sudden dilatation with subsequent contraction, particularly in the longitudinal tracts. Other areas are seen to be serially connected like a string of beads and strung on a longitudinally sectioned bloodvessel.



FIG. 5.—Section of oblongata, midolivary level, of G. W.  $\times 110$ .

At the ponsoblongata transition the vessels are sausage-like and the areas quite numerous. At the level of the inferior quadrigemina the lesions are seen to be arranged in groups as well as single rows, and are large and numerous. One area of special interest is noted in this level; its central part is quite ragged, and contains vessels and torn tissue as though a sudden explosive rending of the structures had occurred. The lesions are equally large and numerous in sections at the level of the superior quadrigemina.

The number and size of the lesions with the number of shocks administered and the length of contacts, are comparatively shown by the following table:

	Shocks.	Total duration.	
Case I. J. B. . . . .	2	1.12	lesions not of the best.
Case II. M. E. . . . .	2	1.09	lesions, average number and size.
Case III. G. G. . . . .	3	1.21	lesions most numerous but not so large as in Case V.
Case IV. A. S. . . . .	4	1.22	fewest and smallest lesions.
Case V. G. W. . . . .	2	1.16	best examples of lesions.

One can only guess at the mode of formation of these lesions. It seems inconceivable that they could be due to sudden momentary dilatations of the bloodvessels themselves. The bead-like arrangement of the lesions along the bloodvessels, the condensation zone limiting each lesion, and the radially disposed fibers and torn tissue would seem to indicate a sudden liberation of the bubbles of gas due to the electrolytic properties of the current as it seeks the paths of the least resistance along the vessels. The maximum number of lesions are found in the most constricted parts of the brain stem in the path of the current, and are most numerous along the longitudinal fiber tracts and bloodvessels.

Since we made mention of our observations in April, 1908, we have noted similar lesions produced in the course of experiments conducted by Sir Victor Horsley and R. H. Clarke.<sup>2</sup>

## HOSPITALS AND TYPHOID CARRIERS.<sup>1</sup>

BY JOHN W. BRANNAN, M.D.,

NEW YORK.

DURING the last two years an increasing amount of attention has been called to the danger to the public health of typhoid carriers, and to the importance of their recognition and control. In August of last year, Meakins,<sup>2</sup> of Montreal, in an exhaustive article on the subject, urged that in our general hospitals, where at least 50 per cent. of the cases of typhoid fever are treated, every case of the disease should be examined bacteriologically during convalescence, and should be kept in the hospital or under strict observation and be treated by homologous vaccines until the excreta were free of typhoid bacilli. Meakins further advised that patients under the care of physicians in private practice should be watched and examined from time to time by officials of the board of health. Impressed by the suggestion of the Canadian

<sup>2</sup> Brain, Part CXXXI, vol. xxxi.

<sup>1</sup> Read at the annual meeting of the Association of the American Physicians, May 15, 1912.

<sup>2</sup> Canadian Med. Assoc. Journal, 1911, p. 711.



writer, I requested Dr. Norris, the director of laboratories in Bellevue and its allied hospitals, to have the feces and urine of all cases of typhoid fever examined during convalescence. This work was begun in September, 1911, and has continued up to the present time. One hundred and nineteen cases in all have been examined, and of these, 15, or 12.6 per cent., had typhoid bacilli in either the feces or the urine or in both. An average of two examinations was made in each case. Forty-eight cases were also examined during the active stage, with a positive result in 10, or in 20.83 per cent. From these figures it appears that about 1 case in 5 gave positive findings during the active stage of the disease, but only 1 in 8 cases by the time they had arrived at convalescence. All patients with the exception of two were bacteriologically free before they left the hospital. These two patients were discharged inadvertently. Their names and addresses and occupations were sent to the Board of Health, though not as promptly as might be wished, as the mistake was not discovered for some time. Our own social service department is also endeavoring to trace them in order that we may make further examinations, if possible, and determine if they are still carriers. At present no typhoid patient is discharged from any of the hospitals in the department except with the approval of the general medical superintendent. We have found no great difficulty in holding patients until they are presumably bacteria free, at least two successive negative examinations being required in every case.

It may be urged that patients discharged as bacteria free after only two examinations with negative results are still potential carriers and would prove to be actually such on further examination. It is believed, however, that this measure of precaution will serve to arrest the great majority. As the work progresses and our methods improve with experience, we shall no doubt be able to increase the number of examinations, at least in those cases that have given positive results at some time in the course of the disease. Dr. Norris is trying to devise some method of securing the bile, which may enable us to arrive at more exact conclusions. Dr. William Hallock Park has also some such procedure in view.

There is one measure at least that we can take to guard the public health against infection by typhoid carriers, either actual or potential, and that is to instruct them in the simple rules of cleanliness. This we should do with all cases of typhoid fever when they leave the hospital or pass from our observation in private practice, but particularly should we do this in the case of those who have shown themselves to be at least transitory carriers. These who are engaged in the preparation or distribution of food should be doubly warned in this regard. We are now preparing a leaflet of instructions to be given to each patient on discharge from the hospital. It would be well, of course, to prevent such

persons from following occupations involving the handling of food or drink; but this in many instances would probably be impossible, particularly in this country. At all events, this is the province of the Board of Health, not of the hospital. It is for us to instruct the patient and give notice to the health authorities, that they may take the necessary measures to protect the public. It may be of interest to note the proportion of those engaged in occupations in which they were liable to infect others. In the 140 different individuals who form the subject of this study there were 14 housewives, 3 nurses, 3 waiters, 2 cooks, 1 orderly, 1 butler, and 1 baker—25 in all. One has but to read this list to see how impossible it would be to compel any considerable number to change their occupation. Hence the importance of instructing them both orally and in writing how to avoid conveying infection.

Regulations for the control of typhoid carriers have been enforced in some countries of Europe for a number of years. In the south-western provinces of Germany there is probably no case of typhoid fever released from observation until the bacteriological examination of the feces and urine has proved negative. In England also typhoid carriers receive a great deal of attention, especially in the English army. After treatment for a period of three months, if it is found that the soldiers are still carriers, they are given the opportunity of entering the hospital or of being discharged. In case of discharge, notification is sent to the medical officer of health of the district in which the soldier is going to reside. In the service in India two convalescent depots were established several years ago, to which the convalescents of certain military stations are sent. After the opening of these depots, namely, Wellington and Naini Tal, it was found that the admissions of typhoid fever from all stations which sent their convalescents there show a reduction of 9 per cent., in 1908, from the figures for the previous year, whereas the remaining stations show an increase of 26.6 per cent.

In the endeavor to sterilize typhoid carriers various methods of treatment have been tried, such as the use of lactic acid bacilli, acidifying the urine, the administration of antiseptics, the use of the x-rays, and the employment of vaccine. The surgeons<sup>3</sup> of the English army report the following results from the use of these five different means of treatment: (1) Lactic acid bacilli cause only a temporary disappearance of the typhoid bacilli. (2) Acidifying the urine fails to cure typhoid bacilluria. (3) The administration of antiseptics invariably brings about a decided diminution in the number of bacilli both in fecal and in urinary carriers. This effect is much more marked when the maximum contact of the antiseptics with the bacilli is obtained by combining the treatment with low diet and aperients in the case of "fecal," and with

<sup>3</sup> Cummins, Jour. Royal Army Med. Corps, London, 1910, xiv, 268-384.

diuretics in the case of "urinary" carriers. (4) The use of  $x$ -rays in the case of gall-bladder infection seems to have definite beneficial results. (5) Vaccines, like the lactic acid bacilli, cause only temporary disappearance of typhoid bacilli. It is suggested that the treatment by vaccines might have a better chance of success if combined with diuretics in the case of "urinary" carriers, and with  $x$ -ray treatment in gall-bladder cases. Sir Almroth Wright has pointed out that a vaccine is more likely to be efficient when the local conditions are so altered as to permit the fullest possible contact between the bacteriolytic products in the blood and the bacteria involved.

Other observers have had better results with vaccines than the English army surgeons. Some have reported permanent cures in cases of long standing, notably Meakins<sup>4</sup> in 2 cases described in detail, 1 of chronic bacilluria of twelve years' duration, the other one of chronic suppurative cholecystitis with gallstones of eight years' duration. At Bellevue we have as yet had to do only with transitory carriers, but Dr. Norris is prepared to use autogenous vaccination when occasion arises.

In conclusion, I am glad to add that these investigations have not proved burdensome to our pathological department, nor have they interfered with the regular routine of the laboratory. The clinical side of the problem presents somewhat greater difficulties, as we have to deal with the changing house staffs of four different hospitals, and it is not always easy to secure their effective coöperation. Gradually, however, even these difficulties are being overcome, and we may reasonably expect that with patience and persistence and good will on all sides they will give us less and less trouble in the future.

---

## THE THERAPEUTIC USE OF VACCINES IN TYPHOID FEVER.<sup>1</sup>

BY JAMES G. CALLISON, M.D.,

PATHOLOGIST, MANHATTAN EYE, EAR, AND THROAT HOSPITAL, NEW YORK.

VACCINES have an unquestioned value in the prevention of typhoid fever. This is evidenced by the experience of various military organizations, and especially the maneuver division<sup>2</sup> of the United States Army in camp in Texas and along the Mexican

<sup>4</sup> Canadian Med. Assoc. Jour., 1911, p. 496.

<sup>1</sup> Read before the New York Academy of Medicine, Section on Pediatrics, being the joint meeting with the Philadelphia Pediatric Society and the New England Pediatric Society.

<sup>2</sup> J. R. Keen, Jour. Amer. Med. Assoc., 1911, lvii, 713 and 714.

border during the summer of 1911. The advisability of their therapeutic employment is as yet, however, an open question. That they have a value is borne out by the testimony of nearly everyone who has reported a series of cases of typhoid fever treated with vaccines as well as by my personal experience. Possibly lack of experience is the most usual cause of failure to resort to their use. I have also heard doubts expressed by some physicians who had treated cases of typhoid fever with vaccines, but who expected them to act as an antitoxin. That the action is different from this is an important point to remember. Vaccines give rise to a slowly initiated, gradual production of antibodies.

In using typhoid vaccines therapeutically, success or failure must be judged in the light of the reaction of living tissue to injections of dead typhoid bacilli. This reaction (the production of opsonins and agglutinins in healthy individuals) has been carefully worked out by Russell and others. According to Russell the response is quite constant, and follows the same curve as is observed after the introduction of any antigen. He has shown that for a period varying between five and eleven days (average eight days) there is no production of opsonins and agglutinins; that from that time until about the twenty-fifth day there is a very rapid production of antibodies, so that these are present in great concentration. This is the result in a normal individual. In the therapeutic use of vaccines, if there is to be any beneficial effect on the temperature curve, it must follow closely the same physiological reaction; for the physiology of the individual or of his component cells is not qualitatively altered. In other words, theoretically, an interval of from five to eleven days should intervene between the first inoculation and any production of antibodies in response to that injection. Following this, there should be a more rapid drop in the temperature curve when the protective substances produced by the inoculation are added to those produced by the infection present. There will, however, be this difference: The reaction of immunity has already been initiated by the existing infection, and the reaction in response to the vaccination will come more quickly than in a normal individual, and the interval between the inoculation and its response will be shortened. This point is shown in the accompanying charts.

In all, I have treated 38 cases of typhoid with vaccines, 24 of which I have previously reported. In these 38 cases there have been 5 deaths and 1 relapse, with an unusual absence of complications. The causes of death were a femoral phlebitis and its sequelæ, a double lobar pneumonia, a meningococcus septicemia, a ruptured spleen, and asthenia. Ultimate conclusions, however, should be drawn from a large number of cases rather than from an individual series.

As illustrative of the changes in the temperature curve in vaccine-treated patients six charts are shown. These changes are to be

day, ten days after the initial inoculation. The Widal reaction, which did not become positive until the nineteenth day of the disease, was positive at a dilution of 1 to 3200 eleven days after the first vaccine injection.

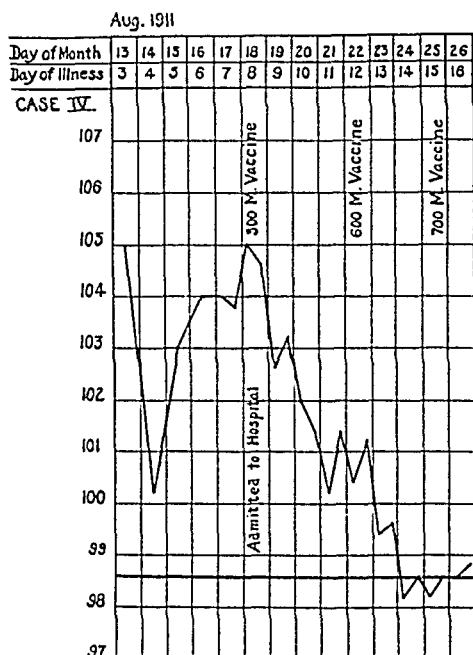


CHART II.—Temperature curve of Case IV after vaccine treatment.

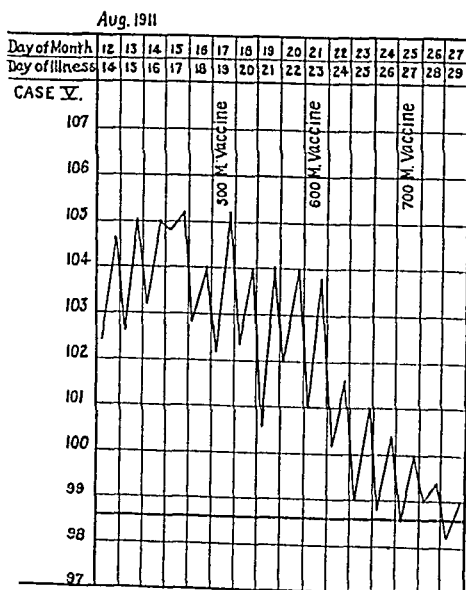


CHART III.—Effect of vaccines on temperature of Case V.

CASE VII.—Mr. J. R., aged sixteen years. An apparently average case of mild typhoid, with no well-marked benefit from the vaccines. The attack ran a text-book course. The chart is self-explanatory.



CASE X.—Master A. R., aged two and a half years, weight 25 pounds. The patient was admitted on the fifth day of the disease, and the first inoculation was on the seventh day. The temperature became normal on the fifteenth day, eight days after the first inoculation. Simultaneously both tympanic membranes ruptured and discharged.

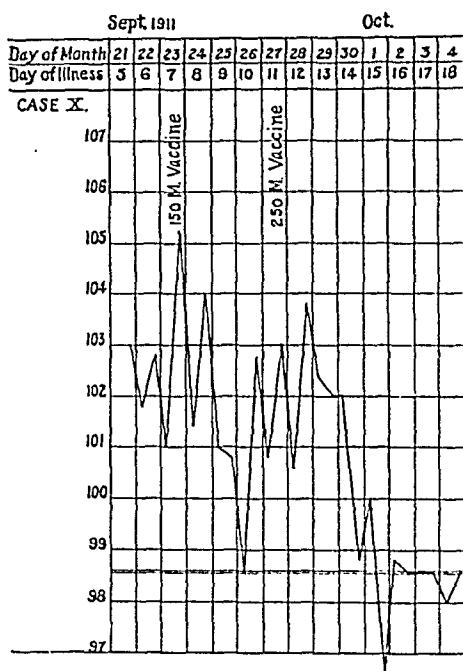


CHART VI.—Temperature curve of Case X, which reached normal on the fifteenth day, eight days after first inoculation.

These charts show a marked change in the temperature curve at a time corresponding to the beginning rapid production of opsonins and agglutinins in the healthy individual following prophylactic inoculation. This change in the temperature occurs so frequently in typhoid cases treated with vaccines that it seems to be more than a coincidence and suggests that the vaccine has played a part in shortening the course of the disease. Accompanying this change in the temperature curve and slightly antedating it, there is an even more marked change in the clinical appearance of the patients. They lose the "typhoid facies," appear bright, and take an interest in what is going on about them. The appetite returns sooner than in patients on ordinary or routine treatment, and they sleep better. There is also a less number of relapses in patients receiving vaccine treatment, and complications seem to be lessened in a way not always easy of explanation.

In the illustrative charts shown there is a similar response to the vaccines in all cases, early and late, with the difference, if there is any, in favor of the early cases. This fact emphasizes the importance of making every effort to secure the earliest possible deter-

mination of the infection, so that treatment may be instituted early. Of the various diagnostic procedures now in use and available for the clinician, blood cultures give the earliest positive information and this should be resorted to whenever possible.

The contraindications to the use of vaccines in typhoid fever have not so far been worked out. Certainly, severe clinical manifestations do not forbid the use of this form of therapy. In some of my cases the prognosis has been of the gravest form, yet the patients responded in a most satisfactory manner. For instance, one patient was suffering from a severe intercurrent nephritis, face edematous, expression dull, urinary findings bad; yet she improved rapidly under vaccines in large doses. Another patient, a bartender, was wildly delirious and constant restraint was necessary. The temperature was running between 104° and 105° F. He was given a dose of 500,000,000 typhoid vaccine, and on the fifth day thereafter the temperature fell to 102.4° F., and he was rational, quiet, and appeared bright. A few hours later he died from internal hemorrhage from a ruptured spleen, which at autopsy weighed 1030 grams. A third patient was in dull delirium, passing urine and feces involuntarily, temperature around 105° F., with a rise of as much as one degree following cold sponging. He made a highly satisfactory recovery after large doses of vaccine—2,000,000,000 in six days' time.

I have recently published<sup>3</sup> a full discussion of vaccines in typhoid fever, with a summary of reported cases, to which those who wish a full presentation are referred. At that time I was able to collect 323 cases of typhoid fever treated with vaccines, with 17 deaths, or 5.2 per cent.; and 20 relapses, or 6.2 per cent. Since that time Meakin and Foster,<sup>4</sup> of Montreal, have reported a series of 41 cases, with the following results in the vaccine cases, embracing one service in the hospital, as compared with the remainder of the hospital: Deaths, vaccine cases, 2.4 per cent.; routine, 10 per cent. Relapses, vaccine cases, 2.4 per cent.; routine, 13 per cent. Complications, vaccine cases, 5 per cent.; routine, 42 per cent. Duration of fever, vaccine cases, twenty-eight days; routine, 37; decrease, nine days. Seventeen cases were vaccinated during the first two weeks and of those only three required a second inoculation. The average duration of fever in the remaining 14 cases were seventeen days. In all, 26 cases received one dose, and the average duration of fever after this inoculation was five days. Eleven cases received two injections, and the average duration of fever after vaccine treatment was instituted, was twelve days. Only 4 of the 41 cases received more than two inoculations. These patients received the largest dosage so far reported. The initial dose was 1,000,000,000. Eight

<sup>3</sup> The Vaccine Treatment of Typhoid Fever, Med. Record, 1911, lxxix, 1129 to 1139, 1161. (This gives a complete bibliography up to that date.) Prophylactic Inoculation and Vaccine Treatment in Typhoid Fever, Post-Graduate, 1911, xxvi, 718 to 740.

<sup>4</sup> Treatment of Typhoid Fever, Canadian Med. Assoc. Jour. (Toronto, 1911), i, 496 to 502.



days later, if required, a second dose of 1,500,000,000 was given and if at the end of a second eight-day period the patient was still running a febrile course, a third injection of 2,000,000,000 was given. The results were certainly most satisfactory. In many of their cases the temperature terminated so rapidly as almost to be by crisis. As to the influence of vaccines on the toxemia, their testimony is equally positive and in accord with the opinion of others. They say: "The beneficial influence of the vaccines on the toxic symptoms was almost constant. In some cases the toxemia diminished out of proportion to the drop in temperature, but in the majority these two conditions were parallel. It may be stated at this time that in no case did any increase in the toxic symptoms appear after the administration of the vaccine."

Elliott<sup>5</sup> treated 3 cases of typhoid fever with vaccines. No facts are given, but he was so well pleased with the results that he expects in future to treat all cases seen early in this way.

Courmont<sup>6</sup> treated 39 cases of typhoid fever with vaccines, using daily two rectal injections of 100 c.c. of killed bouillon culture. There were 2 deaths in the treated cases, or 5 per cent., as against 20 deaths in 171 untreated cases, or 11.6 per cent. "Many cases were materially shortened, defervescence occurring prematurely and unexpectedly." Eight patients relapsed, but all were cured.

Sadler<sup>7</sup> used vaccines in 52 cases of enteric fever, giving an initial injection of 2,000,000 (*sic*) and a later one of 1,000,000 (*sic*). It seemed incredible that he should use so small a dosage after familiarizing himself with the declaration of Smallman<sup>8</sup> that 300,000,000 is the minimum efficient dose. There were 9 deaths in the 52 cases. He admits that the death rate was not reduced, but thinks the patients were otherwise much benefited. He complains that the appetite was stimulated before the condition of the patient justified him in increasing the diet.

Pollack<sup>9</sup> used an autogenous vaccine in a case of typhoid fever complicated by hemorrhages before vaccination was instituted. Improvement began on the eighth day after the first inoculation, but was slow. The case was later complicated by an attack of parotitis.

Renaud<sup>10</sup> treated a variety of conditions with typhoid vaccine. He used a bouillon culture killed by ultraviolet rays. Among his patients was one case of typhoid fever. The patient made a rapid recovery.

<sup>5</sup> Vaccine Therapy in Typhoid, Southern Med. Jour. (Nashville), v, 1-7, abst. Jour. Amer. Med. Assoc., 1911, lvii, 1861.

<sup>6</sup> Treatment of Typhoid Fever by Rectal Injections of Killed Cultures of Eberth's Bacillus. Paris Letter, Jour. Amer. Med. Assoc. (1912), lviii, 1868.

<sup>7</sup> Quarterly Jour. Med., 1911, v, 193-228.

<sup>8</sup> Jour. Royal Army Med. Corps, London, 1909, xii, 136.

<sup>9</sup> Ibid., 1911, xvi, 653.

<sup>10</sup> Presse Médicale, 1911, xix, 665-672.

O'Connor<sup>11</sup> treated a mild case of typhoid with vaccine. The patient made a speedy recovery.

Rosenberger<sup>12</sup> used an autogenous vaccine in a case of typhoid osteomyelitis that had persisted for one year. A cure was obtained in six weeks.

Sharpless<sup>13</sup> treated a case of typhoid periostitis that had persisted for six years. A cure was effected in about two weeks.

Leishman<sup>14</sup> used typhoid vaccine in an unspecified number of cases of typhoid fever. He began this work with a small dose, but cautiously increased this until the initial dose was 50,000,000. He says: "The number of cases so treated is too small to base any general conclusions on, but all who had to do with the patients thought they had benefited greatly. The enteric facies disappeared, the patients said they felt better, and in two or three cases they even asked that the vaccine should be repeated. . . . In my opinion the vaccine treatment of enteric fever is sound practice, and will grow in favor as time goes on."

In addition to the 24 cases already reported by me, I have treated 14 cases, with 2 deaths and no relapse. The deaths were the case of ruptured spleen referred to above, and a patient in whom death was due to asthenia. The dosage I have been using in this series of cases was an initial injection of 500,000,000, repeated at four-day intervals as long as required, and increasing the dose 100,000,000 at each subsequent injection. This gives a total dose similar to the total dosage of Meakin and Foster, as I give half their dose at half the interval. I believe this to be the better practice. I have continued using a stock vaccine, as it causes less local reaction and is less toxic than an autogenous vaccine. It is as efficient a producer of bactericidal substances (opsonins and bacteriolysins) as the more recently isolated strains, and has fewer undersirable side actions.

The vaccines are given in the same way as any hypodermic medication, and the injections are made just under the skin over the insertion of the deltoid or over the tensor vaginæ femoris. Any spot may be selected that is rich in connective tissue and not called into too active motion. The local reaction is essentially the same in prophylactic vaccination and therapeutic inoculation, and consists of redness, swelling, and a brawny induration and is painful on pressure. This passes away in about twenty-four hours and the tissues rapidly return to normal. I am accustomed to warn patients that the arm is going to be very sore, an indication that the medicine is beginning to take effect. In the therapeutic use of typhoid vaccine the systemic reaction can be ignored. In very few of the patients I have treated has there been a rise of temperature

<sup>11</sup> Kentucky Med. Jour., 1911, ix, 978-980.      <sup>12</sup> New York Med. Jour., 1911, xciii, 927.

<sup>13</sup> Jour. Amer. Med. Assoc., 1912, lviii, 1114.

<sup>14</sup> Glasgow Med. Jour. (Glasgow, 1912), lxxvii, 401-410, abs. Jour. Amer. Med. Assoc., (1912), lix, 311.

frankly due to the vaccine, and in none has there been an aggravation of the clinical picture.

Case No.	Patient.	Sex.	Age.	Day of disease.	Date of inoculations.	Amount of vaccine given.	Febrile days after first inoculation.	
1	A. Q.	M.	28	8	June 8	500,000,000	5	Death from ruptured spleen. Post-Graduate Hospital. Service of Dr. Edward Quintard.
2	T. L.	M.	42	14	July 13 July 17 July 20 July 24 July 28 Aug. 1	500,000,000 600,000,000 700,000,000 800,000,000 900,000,000 1,000,000,000	30	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
3	T. K.	F.	14	14	July 27 Aug. 2	300,000,000 400,000,000	8	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
4	F. B.	M.	18	7	Aug. 18 Aug. 22 Aug. 25	500,000,000 600,000,000 700,000,000	6	Uneventful course. Cure. Post-Graduate Hospital. Private patient of Dr. John Welzmler.
5	H. L.	M.	22	20	Aug. 17 Aug. 21 Aug. 25	500,000,000 600,000,000 700,000,000	9	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
6	J. G.	M.	13	9	Sept. 13 Sept. 18 Sept. 23 Oct. 4	300,000,000 500,000,000 600,000,000 1,000,000,000	23	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
7	J. R.	M.	16	19	Sept. 20 Sept. 25 Sept. 29 Oct. 4	500,000,000 600,000,000 800,000,000 1,000,000,000	17	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
8	E. K.	M.	19	10	Sept. 20 Sept. 25 Sept. 29 Oct. 4	500,000,000 600,000,000 800,000,000 1,000,000,000	23	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
9	M. R.	F.	17	7	Sept. 23 Sept. 27 Oct. 2	500,000,000 600,000,000 700,000,000	10	Uneventful course. Cure. Post-Graduate Hospital. Service of Dr. Edward Quintard.
10	A. R.	M.	2½	7	Sept. 23 Sept. 27	150,000,000 250,000,000	8	Cure. Both tympanic membranes ruptured on last febrile day. Post-Graduate Hospital. Service of Dr. Chapin.
11	C. S.	M.	39	13	Oct. 22 Oct. 26	500,000,000 750,000,000 1,000,000,000	14	Cure. Ischiorectal abscess opened on last febrile day. J. Hood Wright Hospital. Service of Dr. Frank H. Daniels.
12	E. M.	F.	20	7	Nov. 7 Nov. 11 Nov. 15	500,000,000 600,000,000 700,000,000	13	Uneventful course. Cure. French Hospital. Private patient. Dr. John Welzmler.
13	D. J.	F.	27	18	Nov. 30 Dec. 4 Dec. 8 Dec. 12	500,000,000 700,000,000 1,000,000,000 1,100,000,000	19	Death due to asthenia. J. Hood Wright Hospital. Service of Dr. H. B. Hanson.
14	C. J.	M.	21	10	Nov. 16 Nov. 21 Nov. 25 Nov. 29	500,000,000 750,000,000 1,000,000,000 1,100,000,000	21	Uneventful course. Cure. J. Hood Wright Hospital. Service of Dr. H. B. Hanson.

There have then been reported so far a total of 475 cases of typhoid treated with vaccines. In this number of cases there have been 31 deaths, or 6.5 per cent., and 31 relapses, or 6.5 per cent. Omitting the 52 cases reported by Sadler, with his absurdly small dosage, we have 423 cases so far reported, with 23 deaths, or 5.4 per cent., and 31 relapses, 6.5 per cent. These cases come from widely separated sources, treated with a great diversity of dosage of vaccine, and with an equal variety of routine treatment, covering a period of three years. This number of cases,

with a death rate of 5.4 per cent., when contrasted with the usual death-rate in typhoid fever of well above 10 per cent., seems to offer a hope of a great reduction in the mortality when the vaccine treatment shall be more generally used and used earlier in the course of the disease. Especially do I wish to contrast this death rate of 5.4 per cent. in vaccine cases with the death rate of 16 per cent. in the Bellevue and allied hospitals in the years 1908, 1909, 1910, and 1911, quoted by Dr. Coleman.<sup>15</sup> Such a contrast must cause the most prejudiced to pause and consider. Any method of treatment that can show so low a percentage of deaths for 423 cases, be it coincidence or scientific achievement, is worthy a further trial.

CONCLUSIONS. 1. Vaccine treatment in typhoid fever will reduce the percentage of deaths and lessen the number of relapses.

2. Complications are less frequent in vaccine-treated cases, and the original attack seems to be shortened in some of the cases.

3. To give the best possible results, vaccine treatment should be instituted as early as it is possible to make a diagnosis, before the patient is exhausted and complications intervene.

## STENOSIS OF THE DUODENUM; A STATISTICAL STUDY WITH THE REPORT OF A NEW CASE.<sup>1</sup>

BY JAMES M. ANDERS, M.D., LL.D.

PROFESSOR OF MEDICINE AND CLINICAL MEDICINE IN THE MEDICO-CHIRURGICAL COLLEGE  
PHILADELPHIA.

CONGENITAL stenosis of the duodenum, which will be omitted from consideration in the present discussion, is properly classed among the rare intestinal conditions. On the other hand, the acquired form occurs less infrequently than has been supposed by internists in the past, and it invariably develops secondarily upon morbid processes either in the duodenum or adjacent organs.

More or less extensive studies of the subject from various viewpoints have been made by Leichtenstern,<sup>2</sup> Perry and Shaw,<sup>3</sup> Wilms,<sup>4</sup> Boas,<sup>5</sup> Laffer<sup>6</sup> and others, but the clinical characteristics of duodenal stenosis have received less study than their importance warrants. A careful consideration of the subject has revealed a somewhat close and interesting relationship between this condition and such common causative affections, as duodenal ulcer and carcinoma, and disease of the head of the pancreas, as well as other adjacent structures.

<sup>15</sup> Jour. Amer. Med. Assoc., 1912, lix, 363.

<sup>1</sup> Read at a meeting of the Association of American Physicians, May 15, 1912.

<sup>2</sup> V. Ziemssen's Handb. der spez. Path. u. Ther., 2 Aufl., Band vii, 2, 411.

<sup>3</sup> Guy's Hospital Reports, 1893, i, 171.

<sup>4</sup> Bruns' Beitr. z. klin. Chir., Tubin., 1897, xviii, 510.

<sup>5</sup> Diseases of the Intestines, 1901, 346.

<sup>6</sup> Ann. Surg., Philadelphia, 1908, xlvii, 1, 390, and 532.

Although numerous examples of stenosis of the duodenum will be presented hereafter, as the result of a statistical investigation, I venture to place the following new case on record, since it embraces certain details of interest and diagnostic value:

Mrs. S. B., aged fifty-six years, was admitted to the Medico-Chirurgical Hospital on Januray 5, 1912, complaining of pain in right hypochondrium and vomiting. Family history negative, excepting death of father from rheumatism. The patient had been in good health prior to four years ago, but since then has had several attacks of illness, which were diagnosticated acute gastritis. Habits were good, although she had used tea freely.

On December 21, 1911, following severe headache and a feeling of weakness, patient was seized with severe pain in right hypochondrium, which lasted about three minutes. This pain was not referred, but recurred three or four times daily, apparently without relation to the time of the ingestion of food, until date of admission to the hospital, and was somewhat relieved by vomiting. Following the first attack of pain, jaundice was noticed. After coming to the hospital, her condition showed marked improvement for a time; the attacks of pain and vomiting ceased, and the jaundice diminished considerably. There was some tenderness in the right hypochondrium and a small mass was palpable, which did not move with respiration. An x-ray examination did not reveal gallstones, but showed the pylorus to be in relation with the gall-bladder region, suggesting adhesions.

An examination of the urine revealed a trace of albumin, a small amount of bile, a trace of indican, and a few narrow hyaline casts. Cammidge reaction negative. A blood count on Januray 6, 1912, showed: Erythrocytes, 3,860,000; hemoglobin, 80 per cent.; and leukocytes, 11,600. Repeated examinations of the feces gave negative results.

On January 17, 1912, an examination of the gastric contents extracted one hour after a test breakfast, gave the following results: Reaction, acid; total acidity, 60; free HCl, 0.1 per cent.; lactic acid, negative; pepsin, present; starch digestion, stage of erythro-dextrin; occult blood, negative; bile, negative; mucus, a small amount.

Up to this time, the patient's condition had been improving, but now vomiting recurred. There was no recurrence of the pain over the gall-bladder region, but the patient vomited frequently large quantities of bile-stained fluid. On January 23, there occurred a severe chill, and the pulse became more rapid and feeble. The temperature pursued a very irregular course, varying from a sub-normal level to  $101\frac{3}{8}^{\circ}$  F. An examination of the blood at this time, showed a leukocytosis of 25,200; the differential leukocyte count resulted as follows: Polymorphonuclear cells, 81 per cent.; small lymphocytes, 7 per cent.; large lymphocytes, 11 per cent.; and eosinophiles, 1 per cent.

On January 26, Dr. Ernest Laplace operated and found the duodenum markedly adherent to the under surface of the liver, and kinked at the site of adhesions. Situated between the duodenum and the liver was the much shriveled gall-bladder. It was necessary to tear away liver tissue in breaking up the adhesions, leaving an excavation in the liver, considerable hemorrhage resulting. The gall-bladder could not be liberated from the duodenum, and owing to the patient's weakened condition, it was deemed advisable to desist before the operation was completed. The patient died three days later, and necropsy was refused. The stenosis of the duodenum in this case was due partly to the constricting cicatrix of an old ulcer and partly to the kinking occasioned by the adhesions. Among other points of interest presented by this case are compression of the gall-bladder and common duct, apparently due to the adhesions, either old or recent, accompanied by jaundice, and indications of a secondary acute inflammatory process obviously occasioned by perforation of the duodenum at the site of an ulcer.

The further discussion of the subject of duodenal stenosis will be considered here in three aspects: (1) The incidence of the condition, including a collective investigation into the cases recorded in medical literature; (2) the etiologic and pathologic causes, and (3) the diagnosis.

#### 1. THE INCIDENCE OF THE CONDITION, INCLUDING A COLLECTIVE INVESTIGATION INTO THE CASES RECORDED IN MEDICAL LITERATURE.

In 1898, Albu was able to collect only 43 cases from the literature, while Moynihan (1912) reports 56 cases from his own personal experience. I can report a totality of 262 collected cases, Albu's 43 cases, referred to above, were not added to those found in the literature in the present investigations, for the reason that this author's original paper could not be found. It should be stated, however, that 71 instances embraced in my statistics were recorded prior to the publication of Albu's article, and it is quite probable that these include many or all of his collection.

No cases of duodenal disease, which were found recorded in the literature, in which any doubt of actual stenosis existed, and of which there were many, are embraced in my series. In determining the existence of duodenal stenosis, I have been guided by either postmortem evidence or that revealed by operation, with a single exception, in which the notes left no room for doubt as to the diagnosis. The accompanying table (Table 1), which is largely self-explanatory, sets forth the names of the reporters and the references, the pathologic causes, whether the latter are intra- or extraduodenal, and also whether benign or malignant. Again the presence or absence of kinking is noted, and other points of unusual interest will be found in a separate column.

TABLE I.

Reporter.	Reference.	No. of cases.	Cause of stenosis.	Remarks.
A. de Haen	Rationes medendi, 1763, vi, 19	1	Compression by head of pancreas	Nature of pancreatic disease not mentioned.
Fullet	J. Univ. et Hebdom. de med. et de Chir. Prat. Par., 1833, xiii, 33	1	Carcinoma of duodenum	Stomach enormously distended; perforation just below papilla.
Mondiere	Archives generales de Paris, 1836, 2, xii, 134	2	Carcinoma of pancreas	One case showed almost complete obstruction. Pancreas three times natural size in Case 2.
Holscher	Hannoversche Ann. f. d. gesamte Heilkunde 1840, Band v, 350	1	Carcinoma of head of pancreas	Complete for distance of three inches, not admitting goose quill.
Tanner	Prov. Med. Jour., 1842	1	Carcinoma of head of pancreas	Lumen size of goose quill.
Teisser	Jour. de Lyon, Nov. 11, 1847	1	Carcinoma of head of pancreas	Obstruction complete.
Chomel	Gaz. des Hôp., 1852, xxv, 37	1	Carcinoma of duodenum	Stenosis admitting little finger.
Arrachard	Gaz. des Hôp., 1860, 98	1	Carcinoma of duodenum	Stenosis almost complete.
Haley	Pacific Med. and Surg. Jour., San Francisco, 1873, 4, vii, 136	1	Carcinoma of duodenum	Stomach greatly distended; growth involving entire duodenum between pylorus and papilla.
Markoe	Tr. N. Y. Path. Soc., 1876, i, 265	1	Carcinoma of duodenum	Carcinoma six inches below pylorus, stercoraceous vomiting
Reynolds	Tr. N. Y. Path. Soc., 1876, i, 266	1	Carcinoma of duodenum	Stomach dilated; vomited large quantities.
Descroizille	France Med., 1876	1	Carcinoma of duodenum	Stenosis complete.
Salomon	Charite Annalen Jahrgang, 1877, iv, 144	1	Carcinoma of head of pancreas	Compressed ductus choledochus; extended into and caused ulceration of duodenum.
Dickinson	New York Med. Jour., 1879, xxx, 149	1	Carcinoma of duodenum	Extending from pylorus to jejunum and reducing duodenum to size of goose quill.
Rosenbach	Verhandlungen der Deut. Gesellsch. f. Chir., xi. Congress, 1882, 135	1	Gangrene of pancreas	Supra-papillary compression by peri-pancreatic abscess.
Cahn	Berl. klin. Woch., 1886, No. 22	1	Sarcoma of lymph glands	Enlargement of retro-peritoneal lymph glands compressing descending portion.
Gerhardi	Virchow's Archives, 1886, Band cvi, 303	1	Carcinoma of head of pancreas.	
Riegel	Zeitschr. f. klin. Med., 1886, xi, 187	1	Gallstone	Gallstone at mouth of common duct, permitting bilious reflux into stomach.
Hagenbuch	Deutsch. Zeitschr. f. Chir., 1887, Band xxvii, I u. 2, 110	1	Cyst of pancreas	
Hagenbuch	Deutsch. Zeitschr. f. Chir., 1887, Band xxvii, I u. 2, 110	1	Hematoma of pancreas	
Mason	Boston City Hospital Records, B. C. H. (unpublished), cclxiii, 26, cclv, 154	1	Carcinoma of duodenum	Opposite papilla: upper two inches duodenum dilated twice usual size.
Whittier	Boston Med. and Surg. Jour., 1889, cxxi, 377	2	Carcinoma of duodenum	In one case growth acted as valve, permitting regurgitation of intestinal contents.
Reiche	Jahrbuch d. Hamburger staatskranken anstalten, 1890, ii, 180, Case I	1	Peritoneal adhesions	Infra-papillary, admitting little finger.
Reiche	Jahrbuch d. Hamburger staatskranken anstalten, 1890, ii, 180, Case II	1	Carcinoma of duodenum	Infra-papillary.
Hochhaus	Berl. klin. Woch., 1891, 17, 409, Case I	1	Pressure of gallstone	Stenosis just below pylorus; perforation of gall-bladder and pressure due to stone; stomach dilated.

TABLE I—(Continued).

Reporter.	Reference.	No. of cases.	Cause of stenosis.	Remarks.
Hochhaus	Berl. klin. Woch., 1891, 17, 409, Case III	1	Kinking due to adhesions	Partial stenosis of pylorus; another stenosis at lower end of duodenum; no tumor nor thickening of duodenum.
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	6	Duodenal ulcer	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	4	Carcinoma of duodenum	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	2	Peritoneal adhesions	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	5	Carcinoma of pancreas	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	1	Carcinoma of liver	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	4	Adhesions about gall-bladder	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	4	Morbid growths	At least, two of these growths were of lymphatic origin.
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	1	Blood clot	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	1	Aneurysm	
Perry and Shaw	Guy's Hospital Reports, 1893, I, 171	1	Kinking	
Lange	Ann. Surg., Phila., 1893, 588	1	Duodenal ulcer	
Fenwick	Cancer and other tumors of Stomach, 1893, 291	2	Carcinoma of duodenum	
Herhold	Charite Ann., 1894, xix	1	Peritoneal adhesions	
Pye-Smith	Tr. of Path. Soc., London, 1894, xiv, 63	1	Carcinoma of duodenum	
Schule	Berl. klin. Woch., 1894, No. 45	1	Gallstone	
Pic	Rev. d. Med., Paris, 1894, 1081; and 1895, 56. Obs., viii	1	Carcinoma of duodenum	"Growth" produced narrowing.
Mikulicz	Arch. f. klin. Chir., 1895, Band li	2	Obstruction by gallstones	Stones in diverticuli of cystic duct, which crossed and compressed duodenum.
Herz	Deutsch. med. Woch., 1896, No. 23, 362, Case I	1	Peritoneal band (tuberculous)	Stenosis complete; tuberculosis of peritoneum.
Herz	Deutsch. med. Woch., 1896, No. 23, 362, Case II	1	Cyst of head of pancreas	Infra-papillary stenosis; stomach not dilated; epigastric distention and pain, both relieved by vomiting of green material
Herz	Deutsch. med. Woch., 1896, No. 24, 379, Case III	1	Gallstone	At first, symptoms of supra-papillary stenosis, later those of infra-papillary, supposedly due to change of position of stone.
Herz	Deutsch. med. Woch., 1896, No. 24, 379, Case IV	1	Carcinoma of duodenum	Infra-papillary stenosis; tumor small, constricting duodenum.
Wilms	Bruns Beit. z. klin. Chir., Tubin, 1897, xviii, 510	1	Carcinoma of tail of pancreas	Caused infra-papillary stenosis.
Rewidzoff	Arch. f. Verdauungskr., Berl., 1898, iv, 369	1	Duodenal ulcer	
Wegele	Munch. med. Woch., 1898, No. 16	1	Obstruction by gallstones	
Aaron	Phila. Med. Jour., Feb. 4, 1899, 280	1	Carcinoma of duodenum	Supra-papillary, encircling duodenum.
Fenwick	Ulcer of Stomach and Duodenum, 1900, 45	2	Duodenal ulcer	
Siegel	Mitt. a. d. Grenz. d. med. w. chir., 1901, viii, 216	2	Carcinoma of pancreas	Infra-papillary.
Boas	Diseases of Intestines, 1901, 303	1	Carcinoma of duodenum	Supra-papillary.
Boas	Diseases of Intestines, 1901, 346	2	Impacted gallstones	Stones protruded from opening of common bile duct.



TABLE I—(Continued).

Remarks.	Reference.	No. of cases.	Cause of stenosis.	Remarks.
Boas	Diseases of Intestines, 1901, 350	2	Duodenal ulcer	Descending portion of duodenum; first portion much dilated.
Ochsner	Tr. Amer. Surg. Assoc., 1905, xxiii, 314	15	Sphincteric action of hypertrophied muscle	Infra-papillary; duodenum dilated; attributed to overaction of muscle, which normally retains chyme until mixed.
Delore	Lyon Med., 1905, cv, 446	1	Duodenal ulcer	Gastric dilatation.
Eve	Brit. Med. Jour., Lond., 1905, ii, 117	1	Duodenal ulcer	Stricture admitting tip of index finger one and one-half inches below pylorus.
Davis	Tr. Chicago Path. Soc., 1905, vi, 345	1	Duodenal ulcer, probably tuberculous	Admitting tip of little finger; stomach dilated; tuberculosis of spleen and epididymis.
Mackenzie	Jour. Amer. Med. Assoc., Aug. 4, 1906, 341	6	Duodenal ulcer	Advocates plastic operation on duodenum in case of "hour-glass contraction."
Eckersdorff	Münch. med. Woch., Oct. 30, 1906	1	Duodenal ulcer	Near pylorus and mistaken clinically for pyloric stenosis.
Gray	Scot. Med. and Surg. Jour., 1907, xx, 35	1	Duodenal ulcer	Mentions stenosis as urgent indication for operation; stenosis may be marked; probe passed with difficulty.
Bernheim	Amer. Med., April, 1907, 234	1	Duodenal ulcer	No operation or autopsy.
Leo	Deutsche. med. Woch., 1907, xxxiii, 1279	1	Not determined	Located below papilla; regurgitation of bile and pancreatic juice into dilated stomach.
Bidwell	The Hospital, Lond., 1907, xlii, 547	1	Duodenal ulcer	Dilatation of stomach.
Laffer	Ann. Surg., Phila., 1908, xlvii, I, 390 and 537	27	Compression by root of mesentery	Found in 120 autopsies of 217 cases of acute dilatation of stomach from literature.
Codman	Boston Med. and Surg. Jour., 1908, clviii	1	Compression by root of mesentery	Causing chronic dilatation of stomach
Deve and Beaurain	Med. Mod., Paris, 1908, xix, 314	1	Compression by root of mesentery	
Mitchell	Tr. Roy. Ac. Med. of Ireland, 1908, xxvi, 76	1	Duodenal ulcer	Stomach dilated.
Berard	Lyon Med., 1909, cxiii, 283	1	Duodenal ulcer	
Sourdel	Bull. et mem. de la Soc. de Anat. de Par., 1910, lxxxv, 230	1	Peritoneal adhesions	Compression by peritoneal adhesions and infected lymphatic glands.
Abadie	Arch. Provin. de Chir., 1910, xix, 287	1	Ovarian cyst	
Cumston	Internat. Clin., 1911, vol. i, 21st ser., 139	1	Adhesions	
Cheney	Amer. Jour. Med. Sci., Mar., 1911, 328	1	Duodenal ulcer	Frequent vomiting.
Johnson	Ann. Surg., 1911, ii, 197	1	Band of adhesions	Operated three months previously for jaundice; repeated attacks of pain, vomiting, and fever.
Burke	Surg., Gyn., and Obstet., October, 1911	1	Duodenal ulcer	Two marked constrictions due to multiple ulcers; and causing hour-glass duodenum.
Mayo, W. J.	Ann. Surg., 1911-12, 313, and personal communication	55	Duodenal ulcer	Occurred in 553 cases of duodenal ulcer.
Bassler and Grant	Amer. Jour. of Gastroenterology, Phila., April, 1912, 15	1	Carcinoma of duodenum	Duodenum thickened and contracted throughout; pancreas enlarged, hard and nodular.
Moynihan	"Duodenal Ulcer," 1912	56	Duodenal ulcer	Found at operation on 287 cases of duodenal ulcer.
Anders	Amer. Jour. Med. Sci., September, 1912, 360.	1	Kinking	Kinking due to adhesions to liver, resulting from duodenal ulcer.

## 2. THE ETIOLOGIC AND PATHOLOGIC CAUSES.

The relative frequency with which stenosis of the duodenum is occasioned by one or other of the primary etiologic conditions, is clearly indicated by the subjoined Table II, since it is believed that my figures furnish a trustworthy basis. It is worthy of note that by far the greater number—215 out of a total of 262 cases—are due to benign conditions, hence are in most cases, at least, amenable to timely surgical treatment. It is a matter of considerable interest that 185 or 70.88 per cent. of the cases were intra-duodenal in origin, and only 76 or 29.12 per cent. extra-duodenal. Cumston<sup>7</sup> found that compression outside the duodenum was by far the most frequent etiologic factor, but according to my own researches, this is true only after the exclusion of duodenal ulcer. Among the extra-duodenal conditions, which operated to produce stenosis were, diseases of the pancreas, compression by the root of the mesentery, adhesions, morbid growths, kinking, gallstones, and of many others a single instance. The principal intra-duodenal causes were ulcer of the duodenum, carcinoma of the duodenum, sphincteric action of the muscular layer and gallstones.

TABLE II.

Causes of stenosis.	Cases.	Percentage.
Ulcer of duodenum . . . . .	140	53.44
Compression by root of mesentery . . . . .	29	11.07
Carcinoma of duodenum . . . . .	23	8.78
Carcinoma of pancreas . . . . .	16	6.11
Sphincteric action of muscular layer of duodenum . . . . .	15	5.73
Adhesions . . . . .	12	4.58
Gallstones . . . . .	9	3.44
Growths . . . . .	4	1.53
Kinking . . . . .	3	1.14
Cysts of pancreas . . . . .	2	0.76
Diseased head of pancreas (nature not mentioned) . . . . .	1	0.38
Hematoma of pancreas . . . . .	1	0.38
Gangrene of pancreas . . . . .	1	0.38
Ovarian cyst . . . . .	1	0.38
Carcinoma of liver . . . . .	1	0.38
Sarcoma of lymph gland . . . . .	1	0.38
Blood clot . . . . .	1	0.38
Aneurysm . . . . .	1	0.38
Not determined . . . . .	1	0.38
Total . . . . .	262	

As stated above, gallstones may also operate by compressing the duodenum from without, *e. g.*, when they occupy a diverticulum in the cystic duct. As a glance at Table I will show, stenosis due to kinking is rare, the numerical proportion being 3 to 262 cases. It is to be recollected, however, that in cases that come to necropsy without previous operation, kinking may not be recognizable, so that the condition may be more common than is indicated by these figures.

## 3. THE DIAGNOSIS

In 1879, Leichtenstern<sup>8</sup> first called attention to certain symptoms, most of which are still recognized as being of major diagnostic importance in stenosis below the ampulla of Vater, namely, the absence of meteorism, the presence of biliary, but never fecal vomiting, the disappearance of the meteorism in the epigastrium after vomiting, and early anuria.

The cases are, for convenience of clinical study, divisible into four groups:

1. Those due principally to kinking of the gut. The diagnosis of duodenal obstruction due to kinking is always difficult, and in most cases quite impossible. The condition may be attended with colicky pains in the epigastrium, which often recur regularly from three to five hours after meals. A duodenal kink is, as was true of my case, occasioned usually by adhesions, which have been produced by an ulcer and other lesions. If the kink be located above the ampulla of Vater, it excites symptoms practically identical with those of pyloric stenosis, with this difference, however, that the former develop acutely, as a rule.

On the other hand, when the topographic position of the kinking is below the ampulla of Vater, as was true of my case, a prominent feature is oft-repeated vomiting of biliary secretion. In respect of its clinical indications, the condition also bears a close resemblance to cholecystitis, and acute stenosis of the same portion of the organ of intra- or extra-duodenal origin, for example, compression of the root of the mesentery as the result of ptosis of the intestines.

In cases due to kinking, as in the case I herewith report, the vomiting may develop suddenly, be oft-repeated, causing shock, and lead to exhaustion of the system. This symptom is less menacing to life in the commoner types of stricture of organic origin, since these induce a more gradual narrowing of the duodenal lumen than kinking. The painful paroxysms referable to the right epigastric region are also more severe and more frequent in acute stenosis than in more slowly developing types of the condition.

The points of difference here referred to (severe pains, more frequent vomiting, shock) may serve to separate the acute condition due to kinking and other causes, from the chronic varieties of stenosis, at least. The early recognition of the nature and significance of the indications of acute obstruction developed upon certain chronic processes is, for the sake of timely operative intervention, of the utmost importance.

2. Supra-papillary duodenal stenosis. When due to the more slowly acting causes than kinking, stenosis above the ampulla of Vater cannot be separated from pyloric constriction, as a rule.

<sup>8</sup> Loc. cit.

In cases in which a contracting ulcer has been the cause of the stenosis, there is usually a clear history of pain from one to several hours after having taken food and that the pain was relieved by vomiting, the latter symptom occurring one to two hours after the pain came on.

3. Stenosis at the ampulla of Vater. Cases in which the obstruction is situated opposite to Vater's ampulla, can be accurately diagnosticated during life, as a rule, although their characteristic symptoms differ in certain particulars from those of either infra- or supra-papillary stenosis. Healed duodenal ulcers, when situated at the orifice of the common duct in the duodenum, may obstruct both the pancreatic and common bile ducts, producing chronic jaundice and progressive emaciation. As pointed out by M. Wilms,<sup>9</sup> obstruction to both the discharge of the pancreatic juice and bile into the duodenum will naturally cause acholic stools with consequent jaundice, and feces rich in fatty elements. The usual gastrointestinal symptoms dependent upon the absence of the biliary and pancreatic secretions, likewise ensue. In these cases marked dilatation of the stomach and of the duodenum above the seat of the stenosis usually occurs.

Boas<sup>10</sup> reports two cases in which the diagnosis of high calculus obstruction of the duodenum was made and verified by operation. In these instances of high incarceration of hepatic calculi in the common duct, the stone partly compressed the duodenum and partly protruded into its lumen. Neither blood nor bile were found in the vomitus and the stomach was dilated. Jaundice was present, and the stools were acholic and contained enormous numbers of fatty acid crystals.

4. Stenosis below the ampulla of Vater. In the more usual chronic type of infra-papillary stenosis of the duodenum, besides pain and vomiting of much biliary matter, other characteristic features are present. For example, the stools may show an absence of the coloring matter of the bile, being clay-colored, and, as Boas has pointed out, may at times present a lime-like consistence. Constipation is marked. Jaundice may be in evidence, although the greater number of the cases recorded, failed to show this symptom.

An analysis of the gastric contents by Boas, Riegel<sup>11</sup> and his pupil Honigmann,<sup>12</sup> and others, showed that free hydrochloric acid is usually absent in the infra-papillary variety, even in non-malignant stenosis; this is evidently ascribable to a free reflux of the alkaline intestinal juices from the duodenum to the stomach. In my case the percentage of free HCl present was about normal, but the gastric contents were not examined during the period of biliary

<sup>9</sup> Loc. cit.

<sup>11</sup> Zeitschr. f. klin. Med., 1886, xi, 187.

<sup>10</sup> Loc. cit.

<sup>12</sup> Berlin. klin. Woch., 1887, No. 18.

vomiting. The absence of two symptoms should be noted here, namely, intestinal meteorism and fecal vomiting.

It may happen, however, as in the case recorded by Lemoine,<sup>13</sup> that duodenal stenosis is bound up with narrowing of the transverse colon, in which cases fecal vomiting may be present. Dilatation of the stomach may occur, but is inconstant in infra-papillary stenosis. The epigastrium may be prominent, but the bowels are empty, as a rule. The epigastric distention subsides promptly, with relief from pain and oppression when present, after free emesis, but reappears in consequence of further regurgitation of bile and pancreatic secretion from the duodenum into the stomach. Herz<sup>14</sup> emphasizes a green color of the vomitus as having much diagnostic significance. This opinion was corroborated by the color appearance of the vomitus in my own case. Stenosis of the jejunum cannot be distinguished from infra-papillary duodenal stenosis. Finally, the latent character of certain cases of partial chronic stenosis of the duodenum must be recollected.

## THE COMPLEMENT-FIXATION TEST IN THE DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC GONOCOCCIC ARTHRITIS.

BY HANS J. SCHWARTZ, M.D.,

INSTRUCTOR IN CLINICAL PATHOLOGY AND CLINICAL INSTRUCTOR IN DERMATOLOGY IN THE  
CORNELL UNIVERSITY MEDICAL SCHOOL, NEW YORK.

(From the Department of Clinical Pathology in the Cornell University Medical School,  
New York City.)

IN a previous paper<sup>1</sup> the writer, in association with McNeil, drew attention to the value of the serum diagnosis of gonococcic infections in general. We there showed that in chronic gonococcic infection, even though limited to the genito-urinary tract, an antibody specific for the gonococcus could be detected in the blood. We showed that this reaction was specific for the gonococcus with the sole exception of meningococcic infection, but did not consider that this fact would detract from the practical value of the test, as there could be little difficulty in distinguishing between the two infections clinically.

We furthermore stated that in our opinion a positive reaction denotes the presence or recent activity in the body of a focus of living gonococci. A negative reaction does not, of course, exclude

<sup>13</sup> Bull. et Mém. de la Soc. Méd. des Hôp. de Paris, 1894, xi, 775.

<sup>14</sup> Deutsch. med. Woch., 1896, No. 23.

<sup>1</sup> AMER. JOUR. MED. SCI., May, 1911.

the possibility of gonococcic infection being present, in the same way as a negative Wassermann reaction does not exclude the possibility of syphilitic infection. In this connection, however, there are two facts to be taken into consideration: (1) In the late lesions of syphilis, in common with the other infective granulomata, there is a distinct tendency for the fibroblasts at the periphery of the lesion to develop into definite connective-tissue cells. We may thus obtain the formation of a more or less well-marked connective-tissue capsule surrounding the lesion. As a result there is arrested activity on the part of the spirochetæ, a less amount of toxin is elaborated, the connective-tissue capsule offers some resistance to the free absorption of the toxins, and, as a result, there may be lessened antibody formation. This condition does not obtain in gonococcic infection, as the lesions here do not tend to become encapsulated. (2) The Wassermann reaction is definitely obscured by recent mercurial treatment. There is no treatment which thus obscures the complement-fixation test for gonococcic infection. On account of these two facts we think that more importance may perhaps be attached to a negative reaction in testing for gonococcic infection than is to be attached to a negative Wassermann test for syphilis.

Finally, we showed that the complement fixation test might be a distinct aid in finally deciding as to whether a patient was cured of his gonococcic infection, inasmuch as the blood test was positive in a certain percentage of cases where other means of diagnosis failed.

The technique of the test is given in detail in our previous paper,<sup>2</sup> and will not be repeated here.

In this paper we propose solely to deal with the application of the complement-fixation test to the differential diagnosis of gonococcic arthritis. The great majority of the cases have been studied in the wards of the second medical division of Bellevue Hospital and in the wards of the New York Hospital. We wish here to express our indebtedness to the attending physicians of the two hospitals for placing their abundant clinical material at our command.

The cases which follow are classified according to the clinical diagnosis throughout:

#### I. GONOCOCCIC ARTHRITIS; GONOCOCCI PRESENT.

CASE I.—Acute arthritis; right knee developed January 18, 1912. Abundant yellow vaginal discharge, in which gonococci were found; first noticed on January 21. Complement-fixation test made February 1 was strongly positive.

<sup>2</sup> Loc. cit.

CASE II.—Urethral discharge for two months; gonococci still present. Acute arthritis of both ankles; tenderness about the knees and at the lumbosacral junction present for nine days. Complement-fixation test positive. Symptoms promptly relieved by antgonococcic serum.

CASE III.—Male, aged twenty-two years. Urethral discharge for three weeks. Gonococci still present. Acute arthritis of both knees and ankles for eight days, accompanied by chills, fever, and sweating. Temperature reached 105° F. Blood examination showed 10,600 leukocytes, with 82 per cent. polynuclears. Widal and blood cultures negative. Complement-fixation test positive on August 12 (twenty-third day). Temperature gradually fell to normal, and patient was discharged from the hospital six days later, all symptoms having disappeared.

CASE IV.—Gonorrhea for three weeks; gonococci still present. Acute arthritis of left knee for three days. Complement-fixation test strongly positive. Much improvement on antgonococcic serum.

CASE V.—Gonorrhea for two months; slight discharge still present, in which gonococci are found. Arthritis of left elbow for four to five weeks. Complement-fixation test strongly positive. Improvement on antgonococcic serum.

CASE VI.—Arthritis of right shoulder, wrist, and sternoclavicular joint for two months. Gonococci present in vaginal smear. Complement-fixation test positive. Cured by vaccine treatment.

CASE VII.—Gonorrhea present for two months; gonococci still present. Five days ago began to suffer from fever, headache, and severe pain in the left wrist. Two days later wrist became swollen, tender, and painful on motion. Complement-fixation test positive. Left hospital three days later, so subsequent course could not be noted.

CASE VIII.—Arthritis of left elbow for six weeks. Gonococci present in vaginal smear. Complement fixation-test positive. Was improved by vaccine treatment.

CASE IX.—Gonorrhea for two months; gonococci still present in prostatic smear. Arthritis of right knee for three weeks. Had been treated with salicylates and colchicum without benefit. Complement-fixation test positive.

CASE X.—Patient has had gonorrhea for five weeks; gonococci still present. Five previous attacks of gonorrhea. Arthritis of left knee for four weeks. Complement-fixation test positive.

CASE XI.—Gonorrhea for six months; gonococci still present. Arthritis of left elbow for one month. Complement-fixation test positive. Improved by vaccine treatment.

CASE XII.—Patient was confined twelve days ago. A few days later arthritis developed, accompanied by fever and sweating. Both knees, both wrists, and left sternoclavicular joint involved.

Treated with salicylates for a few days without benefit. Vaginal smear positive. Complement-fixation test positive. Slow improvement under immobilization and baking.

CASE XIII.—Profuse vaginal discharge began three weeks ago. Arthritis of right knee began three days later, and has persisted in the same joint since. Treated for three weeks by salicylates, but without benefit. Vaginal discharge shows presence of Gram-positive cocci and some Gram-negative intracellular cocci (gonococci?). Complement-fixation test became negative very slowly, but on account of the history it was reported as probably a developing reaction.

Same case one week later. Gonococci definitely established in vaginal discharge. Complement-fixation test strongly positive.

CASE XIV.—Male, aged fifty-four years. Admitted to hospital December 7, 1911. Contracted gonorrhea three years ago and has had morning drop from time to time since. Present illness began five days before admission to the hospital, with a severe chill, fever, and pain in the right ankle; later, the right knee and shoulder, and still later in the other joints, so that on admission to the hospital practically all the large joints of the body were involved, being red, swollen, and tender. The urine contained a great many pus cells. The patient was given salicylates, colchicum, and salol from admission until June 3, with practically no improvement. The temperature ranged from 99° F. to 100.8° F. and the joint symptoms remained practically unchanged. About this time the patient first admitted having contracted a new gonorrhea some three or four days before the onset of his present illness. Urethral smear revealed the presence of gonococci. Treatment with gonococci vaccine was now begun and continued until the patient left the hospital, September 5. The initial dose was 50,000,000, and a gradually increasing dose was given every four to five days until a dose of 150,000,000 was reached. Under the treatment the temperature gradually dropped to normal and the joints gradually improved, so that when the patient left the hospital the inflammatory symptoms had entirely disappeared, only a certain amount of stiffness remaining. The blood was negative on the thirteenth, twenty-third, and thirty-sixth days of the disease. It was positive on the sixty-first day.

CASE XV.—Patient first noticed urethral discharge February 2. Acute arthritis of the right knee developed February 11, followed by involvement of the hip and ankle. On admission to hospital, February 16, patient had an acute multiple arthritis. The temperature ranged from 102° to 104° F. Profuse urethral discharge was present, in which abundant gonococci were found. White blood cells, 27,800. Polynuclears, 84 per cent. Was put on salicylic acid, gr. xx, and sodium bicarbonate, gr. xl, four times a day.



February 19: Blood culture and complement fixation were both negative.

February 21: White blood cells, 7500; polynuclears, 65 per cent. The temperature was still ranging between 102° and 104° F., and there was little change in the joint symptoms.

February 27: Complement-fixation test was strongly positive. The patient was put on gonococcic vaccine.

CASE XVI.—Admitted to hospital October 14, 1911. The patient had gonorrhea eight years ago, lasting three months. One week after the gonorrhea began "rheumatism" of the right knee and ankle developed, which also lasted three months. No other joints were involved.

October 4: First noticed urethral discharge.

October 8: Right ankle and hip became painful, and the next day the ankle was swollen and tender.

October 15: Urethral smear showed abundant gonococci.

October 16: Blood culture and complement fixation test strongly positive for gonococcus. The patient was put on vaccine treatment, with resultant improvement.

CASE XVII.—Acute arthritis of right knee for six weeks. No other joints have been involved. Venereal history denied, but intra- and extra-cellular, Gram-negative, biscuit-shaped diplococci were found in cervical smear. Complement-fixation test was strongly positive.

REMARKS. In Cases I and XVI the reaction was positive on apparently the twelfth and thirteenth days of the disease respectively. We are, however, inclined to doubt the accuracy of the patient's statements in these two instances, inasmuch as our experience with the test so far has been that the reaction does not appear until the latter part of the third or the beginning of the fourth week. In support of this we would call attention to Cases XIII and XV. In Case XIII the reaction was negative on the twenty-first day of the disease, but became negative so slowly that it was reported as probably a developing reaction. Another examination made on the twenty-eighth day of the disease was strongly positive. In Case XV the reaction was negative on the seventeenth day of the disease and strongly positive on the twenty-fifth day. In Case XIV the reaction was negative on the thirteenth, twenty-third, and thirty-sixth days of the disease. It did not become positive until some time between the thirty-sixth and sixty-first day of the disease. On the sixty-first day of the disease the reaction was positive, but by that time the patient had received eight injections of gonococcic vaccine. The case was a very protracted one, recovery being exceedingly slow. The patient's resisting power to the gonococcus was apparently very low, as evidenced by the clinical course and the tardy development of antibodies.

This case is classified as negative in our statistics on account of the fact that a positive reaction could not be obtained until after the patient had received several injections of gonococcic bacterins. We feel, however, that further study will show such cases to be rare. Similarly, one occasionally obtains a negative Wassermann reaction, even in the presence of active secondary symptoms of syphilis.

In Case XII the date of the gonorrheal infection could not be ascertained. It was probably a case of gonorrhea occurring during pregnancy and remaining latent until the uterus was emptied, when it rapidly spread and became a general blood infection.

All the other cases of this group gave strong positive results, but we wish to emphasize here that a positive reaction is not to be expected earlier than about the beginning of the fourth week from the onset of the specific urethritis.

## II. GONOCOCCIC ARTHRITIS TREATED WITH GONOCOCCIC VACCINE.

Ten cases of gonococcic arthritis under treatment with gonococcic vaccine for varying lengths of time and in varying doses have been examined. All 10 cases gave a strong positive result, as was, of course, to be expected, and goes to show that antibodies specific for the gonococcus are readily produced in the human system. These results really prove nothing as regards the etiology of the cases of arthritis in question. The same results would be obtained in any other form of arthritis or in healthy people after treatment with gonococcic vaccine. The cases are introduced here solely to bring forward the evident fact that the complement-fixation test is of no value in the differential diagnosis of arthritic cases that have recently been treated or are still under treatment with gonococcic vaccine.

## III. CASES CLINICALLY DIAGNOSTICATED AS GONOCOCCIC ARTHRITIS, BUT IN WHICH GONOCOCCI COULD NOT BE FOUND.

### 1. *Cases Giving a Positive Complement-fixation Test*

CASE I.—Acquired gonorrhea two years ago. Says he has had two relapses since. Still has slight morning drop. Arthritis developed shortly after attack of gonorrhea began, left wrist, both knees, and bursa in front of right tendon Achillis being affected. Patient was laid up for three months and has never been free from joint troubles since.

CASE II.—Had gonorrhea twelve years ago. No urethral discharge at present. Prostatic smear not made. Acute arthritis of left knee began January 28, the knee becoming swollen, tender,

and painful. Temperature ranged from 98.2° in morning to 100.2° F. in evening from January 29 to February 4, after that it remained normal until patient was discharged February 21. Blood examination February 1: Leukocytes, 10,100; polynuclears, 82 per cent. Complement-fixation test positive February 1 and 8. Treatment: Sodium salicylate and sodium bicarbonate. Knee still somewhat swollen and painful when patient left the hospital, February 21. No other joints involved.

CASE III.—Gonorrhea began five months ago; no discharge for last three months, but urine still cloudy and containing a considerable number of pus cells. Tenderness, pain, and swelling of both knees and ankles for last six weeks.

CASE IV.—Had gonorrhea seven and three years ago. With each attack of gonorrhea the patient had rheumatoid pains in the body. Present attack of gonorrhea began three months ago and slight morning discharge is still present. Ten to fifteen days after the onset of the present attack of gonorrhea the patient noticed pain in both ankles, joints, and heels. Joints became swollen and painful a few days later, and this condition has persisted since.

CASE V.—Male, aged forty-two years. Admitted to hospital August 3, 1911. Has had gonorrhea several times and has had a stricture for some years. Has suffered from pains in hips, legs, and thighs at intervals for several years. One acute attack of rheumatism in ankles three years ago. For one week has had sudden intermittent pains in hips, knees, and shoulders, and joints are painful on motion. Pus cells in urine; gonococci not found. Treatment: Aspirin, gr. iv, every fourth hour. Still had considerable pain on discharge, August 8, 1911.

CASE VI.—Admitted to the hospital August 11, 1911. Has had gonorrhea seven times, and with each attack a multiple arthritis has developed, the toes, ankles, vertebral, and sternoclavicular joints being involved. The present illness began one week ago with chills and diarrhea. The following day pains developed along the spine and in the feet. The small joints of the feet became slightly swollen and painful, and also pressure on the heels and on the seventh cervical and first dorsal vertebræ. The temperature on admission was 101.5° F., but dropped to normal in a few days. Prostatic smear showed the presence of some pus cells, but gonococci could not be demonstrated.

CASE VII.—Patient first complained of vaginal discharge and burning micturition about August 15. Acute arthritis of left elbow began August 23. Gonococci could not be demonstrated in the vaginal discharge. On September 5 the complement fixation test was positive. The patient was treated by gonococcic bacterins, with slow but ultimate recovery as regards the inflammatory symptoms, though stiffness persisted for a long period. Subsequent blood examinations on September 26 and November 9 were positive

as was, of course, to be expected while the patient was receiving injections.

CASE VIII.—Admitted to the hospital February 29. Gives history of gonorrhea eight year ago. Patient states that ten days ago a urethral discharge appeared, which was followed four days later by an acute arthritis of the right knee and ankle. When admitted to the hospital no discharge could be obtained from the meatus. Smears made from the urethra and prostate revealed very few leukocytes, but no Gram-negative organisms. The complement-fixation test was strongly positive on February 29.

CASE IX.—Patient had gonorrhea four years ago, lasting two months. Recurrence or reinfection one year later and again the following year. With the third attack gonococcic arthritis began and has practically incapacitated him since. The heels, both knees, shoulders, elbows, wrists, and temperomaxillary joints have been at various times affected. Urine is clear, excepting some large pus shreds; after prostatic massage the urine is cloudy and contains many pus cells. Gonococci not found.

REMARKS. Case V did not remain sufficiently long under observation to make the diagnosis absolute. It seems, however, fair to assume that the patient was suffering from the arthralgic type of the disease, in which there are wandering pains about the joints without redness or swelling. These may persist for a long time. Case VII was a typical case of gonococcic vaginitis and arthritis, but gonococci could not be demonstrated in the smears made from the vagina and cervix. It serves to emphasize the well-known fact of the difficulty and uncertainty of diagnosing gonococcic infection in women by means of urethral or cervical smears. Case VIII is of some interest. The patient states that ten days before admission to the hospital a urethral discharge appeared which he looked upon as a fresh gonorrheal infection. Examination at the time of admission, however, showed no urethral discharge. Smears made from the urethra and prostate revealed few leukocytes and no Gram-negative organisms. The blood was strongly positive ten days after the supposed date of infection. Personally we are inclined to doubt the accuracy of the patient's statements, as we have never seen a positive reaction develop so early in the course of the disease. Extended comment on the remaining cases of this group does not seem to be necessary. A study of the individual case records would seem to support the correctness of the clinical and serum diagnosis.

## 2. Cases Giving Negative Complement-fixation Test.

CASE I.—Acute arthritis of right knee began six months ago, the knee becoming greatly swollen and painful. Some time after this a vaginal discharge was first noticed, which has persisted since. On admission to the hospital February 23 the right knee was found to be much swollen and there was marked tenderness

over the patella and the external and internal condyles of the femur. There was a profuse yellow vaginal discharge containing many organisms, but gonococci could not be demonstrated. Temperature normal. No evidence of tuberculosis. Treatment consisted of immobilization, tonics, etc., but with little improvement.

CASE II.—Admitted to hospital May 1, 1911. Patient developed gonorrhea about April 15; was treated for one week, when severe pains in left knee and in metatarsophalangeal joints of both feet developed. He was taken to the hospital on April 23, and remained until April 30, when he was discharged cured. Readmitted May 1 for same trouble, the left knee, metatarsophalangeal joints of both feet, and both heels being tender, painful, and swollen. Urethral discharge present contained many pus cells, but no gonococci could be found. Complement-fixation test negative on May 2. Symptoms subsided rapidly under treatment with salicylic acid and sodium bicarbonate, and patient was discharged May 8.

CASE III.—Male, aged twenty-eight years. Admitted to the hospital August 1. Has had urethritis for eighteen months; still slight discharge from meatus in morning; gonococci not found. Right wrist and left knee became suddenly swollen, hot, painful, and tender seven months ago. Later nearly all joints of body became involved at various times. Began to get better three months ago, but pain and stiffness persisted. On admission to the hospital the right wrist was found swollen, deformed, not painful on motion, but its use limited. Left knee slightly swollen. Nearly all other large joints of body showed same tenderness and limitation of motion, but no swelling. Treatment consisted of aspirin, gr. x, every fourth hour, codliver oil, and iron. Patient complained of very little pain after August 3, and was discharged on August 22, 1911.

CASE IV.—Female, single, aged twenty-eight years. Admitted to hospital December 29, 1911. History of rheumatism in family. Venereal history denied. No previous history of arthritis. For last two months gradually increasing pain in right ankle, so that she had to stop work one month ago. The ankle was swollen, especially at night, less so in the morning. One month ago the left elbow and shoulder began to feel stiff in the morning, but did not become swollen. Slight burning on micturition for last two months. Her present condition shows the right ankle and a distance of two inches above it uniformly swollen; skin hot and dry; tissues soft; no edema; some fluid in joint; active and passive motion painful; no crepitus. Heart normal. No vaginal discharge. Urine contains a few white blood cells. Wassermann reaction negative. Temperature during her stay in the hospital ranged from 98° to 100° F. in the morning and from 101° to 104° F. in the evening, and was irregular in type. Treatment throughout consisted of salicylic acid, aspirin, and strychnine. From January 26 to February 2,

four doses of gonococcic vaccine were given, beginning with 62,000,000 and ending with 100,000,000 without any material influence on the temperature. Patient left the hospital February 3, fairly comfortable, but with still considerable swelling and tenderness of ankle. The temperature was still ranging from 100° F. in the morning to 104° F. in the evening.

REMARKS. On account of the clinical course and prompt response to treatment with salicylates it seems to us that in Case II the clinical diagnosis is perhaps open to question. Even though the diagnosis of gonococcic arthritis and urethritis be accepted, we are not surprised at obtaining a negative complement-fixation test. The blood was taken on the seventeenth day of the disease, and, as a rule, the reaction does not appear so early. Cases I, III, and V are undoubted instances of infectious arthritis. In view of the negative findings as regards gonococci and the complement-fixation test it seems to us that the diagnosis of gonococcic arthritis must be accepted with reserve. A search for some other organism as the etiological factor seems to be indicated. The irregular type of temperature observed in Case V, ranging as it did from 98° to 100° F. in the morning to 101° to 104° F. in the evening throughout the patient's stay in the hospital, seems also to be rather against the diagnosis of gonococcic arthritis.

#### IV. ARTHRITIS DEFORMANS.

1. *Cases Giving a Negative Complement-fixation Test.*—Fifteen typical cases of arthritis deformans are included in this group. All gave a history of chronic deforming arthritis, with acute exacerbations extending over a period of from one to eight years. In all, the small joints of the extremities were chiefly involved, though in many there was also involvement of various other joints, such as the wrists, elbows, knees, ankles, temporomaxillary joints, and cervical vertebræ. The condition varied from slight stiffness, swelling, and deformity in the early cases to marked enlargement of the ends of the bones with almost complete ankylosis and muscular wasting in the more advanced cases. Fourteen of the cases denied a venereal history, and urethral and vaginal smears were negative in all. Two of these cases dated the onset of the arthritis from childbirth some years before, but in neither could any organism be isolated, though they were both probably due to an infectious process beginning at that time. One case showed some thickening of the Fallopian tubes, but smear and culture from the cervix also proved negative. Two cases had had leucorrhœal discharge for some years, but gonococci could not be demonstrated, although many other organisms were present, for example, Gram-negative bacilli and cocci and Gram-positive diplococci.

Another case was that of a female, aged forty-five years, single, and giving no venereal history. Vaginal smear showed no pus cells, but many cocci and bacilli, no Gram-negative diplococci. This patient had an infection of the antrum of Highmore and from this focus the *Bacillus pyocyaneus*, *Bacillus mucosus capsulatus*, and the pseudodiphtheria bacillus were isolated. The patient's serum was tested for complement-fixative bodies, with an antigen prepared from each of these organisms separately. The results were all negative, so none of these organisms could be looked upon as an etiological factor in connection with the arthritis. The bacteriological work in this case was done by Dr. W. Elser, of the Cornell Medical School, who kindly furnished us with the cultures from which the antigens were made.

The only case of arthritis deformans giving a venereal history was a male who had had the arthritis for fourteen years, periods of exacerbation alternating with periods of quiescence. He had had gonorrhea five years and one year previously. At the time the blood examination was made the urine was clear and gonococci could not be demonstrated in a prostatic smear.

#### V. ACUTE RHEUMATIC FEVER.

All of these cases were typical examples of the disease. They were all characterized by sudden onset, high fever, acid sweats, and polyarthritis, with the usual marked tendency to flit from one joint to the other. Many showed cardiac involvement and all yielded promptly to salicylates.

1. *Cases Giving a Negative Complement-fixation Test.* Twenty-three of these cases denied all venereal history and urethral and vaginal smears were negative in all. Four cases gave a definite history of having had gonorrhea, but in none was there any evidence of the disease at the time the blood test was made. They were all males and prostatic smears were negative in all.

2. *Cases Giving a Positive Complement-fixation Test.* One case was a female with profuse vaginal discharge, in which Gram-negative intra-cellular diplococci were found. Another case was a male who had had gonorrhea several times. His prostate was tender on palpation and many pus cells were found in the urine after prostatic massage. There were some Gram-negative extra- and intra-cellular cocci. Finally, there was another female with thick purulent vaginal discharge. Gonococci could not be demonstrated, but clinically the condition was one of gonorrheal endocervicitis. There is little doubt that all 3 patients were suffering from gonorrheal infection as well as acute rheumatic fever. They have been classified as acute rheumatic fever rather than gonococcic arthritis on account of the clinical picture, especially the distinct tendency for the joints to be involved successively and also on account of the prompt

response to treatment with salicylates. These cases have been cited here to emphasize the point that the complement-fixation test merely diagnosticates the presence of gonococcic infection somewhere in the body; but this, of course, does not preclude the possibility of some other infection being present at the same time.

# VI. CASES OF ARTHRITIS IN WHICH NO DEFINITE CLINICAL DIAGNOSIS HAD BEEN MADE AT THE TIME THE BLOOD WAS EXAMINED.

## 1. *Cases Giving a Positive Complement-fixation Test.*

CASE I.—Urethral discharge for one month; slight in amount now; gonococci not found. Acute arthritis of left knee for three days. The diagnosis lay between acute rheumatic fever and gonococcic arthritis. As a result of the positive blood finding the patient was put on antigonococcic serum, with prompt relief.

CASE II.—Case of chronic multiple arthritis. Venereal history present. Urethral and cervical smears negative for gonococcus. Purulent salpingo-oöphoritis found on examination. The complement-fixation test was positive September 7, 1911. A panhysterectomy was done October 11, which was followed by considerable improvement in the joint symptoms. The complement-fixation test was still positive November 9, 1911, which was to be expected, as, in our experience, it takes six to eight weeks for the reaction to disappear from the blood after the focus of infection has been removed.

CASE III.—Female, aged twenty-seven years. Venereal history denied. Has had severe pain and swelling in the left knee for six weeks. No fluctuation could be made out in the joint. Cervix is large and soft; considerable vaginal discharge; gonococci not found. Temperature normal throughout. Treatment consisted of immobilization and baking, but improvement was gradual and slow. Was given antigonococcic serum, after which the pain was distinctly less, but the swelling remained the same, in which condition the patient left the hospital after a stay of five weeks.

CASE IV.—Male, aged twenty years. Venereal history denied, but some shreds were found in the urine. Prostatic smear negative. Acute arthritis of right wrist for three weeks not relieved by salicylates. Was subsequently cured by vaccine treatment.

CASE V.—Acute arthritis of left ankle for one month. Venereal history denied, but shreds were found in the urine. Prostatic smear not made. Had been thoroughly treated for one month with salicylates, colchicin, and potassium iodide, without relief. Dr. W. Gilman Thompson, in consultation, made the diagnosis of gonococcic arthritis, and suggested that a complement-fixation test be made. This turned out to be positive, but the patient was lost sight of shortly afterward so the final result is not known.



CASE VI.—(The following notes are abstracted from Dr. Geo. K. Swinburne's<sup>3</sup> paper). Patient had had a painful arthritis of the knee for eighteen years, during all of which time it had been treated as tuberculous. He had to wear a brace almost constantly, and was frequently laid up in bed for weeks at a time. He gave a history of having had gonorrhea when aged thirteen years and when aged fifteen years his arthritis began. When aged twenty-three years he had a second attack of gonorrhea, which only lasted a short time. The possibility that he was suffering from gonococcic arthritis having been suggested to him, the patient had an x-ray picture taken, which showed that the joint was not a tuberculous one. The patient then consulted an orthopedic surgeon, who stated that the joint looked like a gonococcic arthritis. He then consulted Dr. Geo. K. Swinburne, who kindly referred him to me for a complement-fixation test. This proved to be positive. Dr. Swinburne then put the patient on a course of gonococcic bacterins. Steady improvement began almost at once as regards the pain, and finally resulted in complete cure as regards the inflammatory symptoms, though considerable ankylosis of the knee remained.

CASE VII.—Had gonorrhea twelve years ago; no signs present now; prostatic smear negative. Has had acute arthritis of right knee for three weeks. Cultures from knee-joint negative. After the blood test was made the patient was treated with gonococcic vaccine, which resulted in distinct improvement.

CASE VIII.—Male, aged thirty-seven years. Admitted to the hospital April 4. The patient spoke no English, so no history could be obtained. No urethral discharge; prostatic smear not made. Disease began eight days ago. At present his left elbow is slightly swollen and tender; index, ring, and little fingers of right hand swollen and tender; both knees and ankles tender, but not swollen. Temperature on admission 102° F. The case was at first looked upon as one of acute rheumatic fever and the patient was put on salicylic acid, gr. xx, and sodium bicarbonate, gr. xl., every fourth hour, under which the joint symptoms subsided and the temperature fell to normal on April 7. On the following day the joint symptoms again became worse and the temperature began to rise, reaching 102° F. on April 11. On April 13 the temperature again became normal and remained so until April 22. The joints during this period improved somewhat, but still caused the patient considerable pain. On April 23, while still under salicylates, another relapse began and lasted until May 1. The temperature during this period rose to 102° F., and all the joints become acutely inflamed again. From May 1 the temperature remained normal and the joint symptoms were less severe until the patient left the hospital May 5. He returned, however, a few days later suffering from another relapse,

<sup>3</sup> Arch. Diag., July, 1911.

and was sent to the City Hospital on Blackwell's Island, so the subsequent course is not noted. The complement-fixation test was made on May 2 during a period of quiescence, and the patient left the hospital three days later, so that vaccine or serum treatment was not instituted.

CASE IX.—Female, aged twenty-nine years, single. Has had slight leucorrhea from time to time. None for some months. Venereal history denied. Had slight burning pain on micturition seven to eight weeks ago, which only lasted a few days. About five weeks ago began to suffer from pain in left instep, later in toes, and still later the ankle became red, swollen, and painful. The instep and toes became well, but the ankle has remained affected. No fever, no cough. Has had night sweats since onset of trouble, and has lost considerable weight. Physical examination negative, except as regards the left ankle, which is swollen and tender, especially about the tendo Achillis. No vaginal discharge. Smears made from urethra and cervix negative for gonococcus. X-ray picture showed slight erosion of the tip of the astragalus, which led to the suspicion of the joint being a tuberculous one, and the patient was transferred to the surgical wards. The complement-fixation test was strongly positive.

CASE X.—Female, aged twenty-four years, single. Admitted to the hospital September 25. Previous history negative. Three days before admission the third finger of the left hand and the right wrist became red, swollen, tender, and painful on motion. This condition has persisted without any new joint involvement. The urine contained many leukocytes, but gonococci could not be found in the urethral or cervical smears. The treatment at first consisted of aspirin, gr. x, and sodium bicarbonate, gr. xx, every second hour, but was without any influence on the temperature or joint symptoms. The blood examination was positive on September 28 and on October 8, and the patient was put on gonococcic vaccine. She received seven injections during the period from October 8 to October 30. The initial dose was 10,000,000 and the last one 65,000,000. Under this treatment the temperature, which had been ranging from 98° F. to 100° F., gradually subsided until it reached normal on October 18 and remained so until her discharge. The joint symptoms also distinctly improved, though more or less pain was still present in the wrist when the patient left the hospital December 2.

REMARKS. Case II illustrates the persistence of a positive reaction in the blood for four weeks after the focus of infection had been removed. This is to be expected, as in our experience it takes six to eight weeks for the reaction to disappear from the blood after the toxins responsible for the production of the antibodies have ceased to be elaborated.

In Cases IV and V the patients both absolutely denied venereal

history, but the presence of a few shreds in the urine aroused more than a suspicion that their statements were untrue. In Case IV the subsequent course confirmed the correctness of the blood test. Case V was lost sight of shortly afterward, but there is little doubt that he also was suffering from gonococcic arthritis.

In Case VIII the diagnosis of gonococcic arthritis may seem open to question. On the other hand the distinct tendency to relapse even under heavy doses of salicylates would make one question the diagnosis of acute rheumatic fever. In our opinion the positive complement-fixation test in such a case would justify a course of gonococcic bacterins, and it is unfortunate that this could not be done.

Case IX again illustrates the difficulty and uncertainty of diagnosing gonorrheal infection in women by means of the history or by examination of urethral and cervical smears. In this case there was no vaginal discharge and urethral and cervical smears were negative for gonococci. It was only on close questioning after the positive report on the blood had been made that the patient admitted practising promiscuous sexual intercourse, and said that she had had intercourse shortly before the attack of burning micturition, which occurred seven to eight weeks before her admission to the hospital and two weeks before the onset of her arthritis. It seems fair to conclude, therefore, that the patient contracted gonorrhea at that time and that the joint condition was a gonococcic arthritis.

In Case X also the complement-fixation test gave the only positive proof of gonococcic infection and the correctness of the diagnosis was borne out by the subsequent course.

## 2. Cases Giving a Negative Complement-fixation Test.

CASE I.—Male, aged forty-one years. Venereal infection denied. Admitted December 1. Present illness began four weeks ago with pain in the upper part of the chest, then the left shoulder became painful, swollen, and red. This was followed in turn by the left wrist and elbow, left ankle, hip, and knee. Present condition: Redness, swelling, heat and pain, tenderness, and limitation of motion in the left wrist and both ankle-joints. Pain, tenderness and slight limitation of motion in the left shoulder and the left sternoclavicular joints. In the left hip and knee-joints no crepitation, no bone changes. No urethral discharge; no discharge after prostatic massage. Patient was put on salicylates, but no material improvement had taken place when he left the hospital December 7.

CASE II.—Acute gonococcus urethritis for one week; acute arthritis of right knee for three days. The patient unfortunately left the hospital before the diagnosis could be definitely established.

CASE III.—Rheumatoid affection of the spine for three years; had gonorrhea and prostatitis seven years ago.

CASE IV.—Female, aged thirty years. Patient has suffered from recurring attacks of arthritis of right ankle since aged thirteen years. The attacks recur at intervals of six months and last from one to three weeks. The pain is distinctly worse at night whether the foot has been used much or not. The tenderness is localized to a point over the external malleolus. The present attack has lasted about four weeks. A double salpingectomy was performed two and one-half years ago. Copious vaginal discharge now present; gonococci not found. The diagnosis rested between gonococcic arthritis and tuberculosis, and the complement-fixation test seemed to bear out the latter diagnosis.

CASE V.—A case of chronic deforming arthritis of many years' duration in a child aged thirteen years. Both knees and both elbows were involved. Looked upon as a case of Still's disease.

CASE VI.—Male, aged twenty-nine years. Contracted gonorrhea five years ago. Two months later, before the gonorrhea was cured, rheumatism developed, which lasted four months. Practically all the joints in the body were involved at that time, including the heels. Gonorrhea again three years ago, lasting until two months ago. None since. Present illness began eleven weeks ago and practically all the joints in the body have been affected since. The heels again were affected. On account of this involvement of the heels the possibility of gonococcic arthritis was first considered. The urine was, however, quite clear, prostatic smear was negative for gonococcus, and the complement-fixation test was also negative. The symptoms responded promptly to salicylates, showing that the case was undoubtedly one of subacute rheumatism.

CASE VII.—Patient gave a history of chronic arthritis of the hip-joint for two and one-half years. Venereal history denied; prostatic smear negative for gonococcus.

CASE VIII.—Female, married. Admitted to hospital February 19. No history of venereal disease. Present illness began about six months ago, with acute involvement of the right wrist and metacarpophalangeal joints, both knees and both elbows. Under treatment for "rheumatism" all the joints became well in about two weeks except the left elbow and the left knee, in which the condition has persisted. Both these joints on admission to the hospital were swollen, tender, and contained fluid. No vaginal discharge present. Urethral and cervical smears negative for gonococcus. Gonococcic complement-fixation test and blood culture and Wassermann reaction all negative. The temperature was practically normal from admission until February 25, when a slight rise in temperature took place, ranging from 99° to 101° F., and persisted until the patient left the hospital March 4.

REMARKS. In Case I there was no reason to suppose that the condition was one of gonococcic arthritis. The diagnosis rested between arthritis deformans and subacute rheumatism, but the

patient left the hospital before the diagnosis could be absolutely established.

CASE II was probably one of gonococcic arthritis, but as the gonorrheal infection had only lasted one week when the blood was taken the reaction was, of course, negative. This case also left the hospital before the diagnosis was definitely established.

In Case IV the arthritis began when the patient was aged thirteen years, a fact in itself rather against the diagnosis of gonococcic arthritis. It is, of course, possible that the patient had gonorrheal infection at that time, but there was no history of vaginal discharge until years after the arthritis had begun.

Case VI serves to bring out the point that too much stress must not be laid on involvement of the heel in making the diagnosis of an arthritis, though undoubtedly the majority of the cases of talalgia are of gonorrheal origin.

Case VIII was undoubtedly one of infectious arthritis, but all the evidence was against its being of gonorrheal origin.

#### VII. OTHER JOINT AFFECTIONS.

Three cases of gout, all of whom denied venereal history and in whom prostatic smears were negative, gave a negative complement-fixation test. One case of gout admitted having had gonorrhea four times and had many pus cells in the urine. Gonococci could not be found and the blood test was negative. One case of syphilitic arthritis denying gonorrhea gave a negative gonococcic complement-fixation test and a positive Wassermann reaction. Another case of syphilitic arthritis admitted having had gonorrhea four times, the last time thirteen months ago. Some shreds were present in the urine, but gonococci could not be found. This case also gave a negative gonococcic complement-fixation test and a positive Wassermann reaction. Both cases responded promptly to treatment with Hg and KI. Three cases of multiple infectious arthritis from which the *Streptococcus viridans* was isolated from a local focus of infection gave a negative gonococcic complement-fixation test, as did another case in which a hemolysing streptococcus was isolated from the blood. Finally, in one case of tuberculous arthritis in which venereal history was denied, the prostatic smear was negative. Here a positive von Pirquet reaction was obtained and also a reaction to tuberculin injected subcutaneously. Cultures from the knee-joint were negative. The gonococcic complement-fixation test was also negative.

From our work so far we would state that in our opinion a positive complement-fixation test is an absolute indication of gonococcic infection somewhere in the body.

A positive reaction should not be expected earlier than about the beginning of the fourth week from the onset of the infection.

## SUMMARY.

Clinical diagnosis.	Total number cases.	Positive.		Negative.	
		No.	Per cent.	No.	Per cent.
I. Gonococcic arthritis; gonococci present .	17	16	94.1	1	5.9
II. Gonococcic arthritis, treated with bac- terins .	10	10	100.0	0	0
III. Gonococcic arthritis; gonococci not found	13	9	69.2	4	30.8
IV. Arthritis deformans .	15	0	0	15	100.0
V. Acute rheumatic fever:					
(a) uncomplicated . . . . .	23	0	0	23	100.0
(b) with gonorrhea . . . . .	3	3	100.0	0	0
VI. Cases for diagnosis . . . . .	18	10	55.5	8	44.5
VII. Other joint affections . . . . .	11	0	0	11	100.0

A positive reaction is obtained in a certain number of cases of gonorrhea where bacteriological examination fails. This is especially the case in women.

A negative reaction does not exclude gonococcic infection, but is to be given some weight on account of the reasons detailed earlier.

It is to be remembered that gonorrhea is a common affection in both sexes. This fact should not be lost sight of in interpreting a positive result in connection with any given case of arthritis. A person may suffer from two infections: for example, acute rheumatic fever and gonorrhea, as shown in the preceding records.

Interpreted, however, in the light of the clinical history and clinical findings it seems to us that the complement-fixation test should prove an addition to our means of diagnosis between gonococcus arthritis and other forms of arthritis of obscure etiology.

## A CRITICAL COMMENTARY ON THE FREE EYE INFIRMARY, WITH SUGGESTIONS AS TO REFORMS IN OPHTHALMIC HOSPITALS, DISPENSARIES, AND SCHOOLS.

A COMPILATION FROM CORRESPONDENCE AND OBSERVATION.

BY H. V. WÜRDEMANN, M.D.,

EDITOR "OPHTHALMOLOGY;" ASSOCIATE EDITOR "OPHTHALMIC RECORD;" FORMERLY PROFESSOR  
OF OPHTHALMOLOGY, MARQUETTE UNIVERSITY; CHAIRMAN, SECTION ON OPHTHALMOLOGY,  
AMERICAN MEDICAL ASSOCIATION, 1901, SEATTLE, WASHINGTON.

SUGGESTIONS from several teachers and members of the staffs of ophthalmic institutions inspired an inquiry by the writer into alleged conditions which necessitated correspondence with promi-

ment ophthalmologists and teachers in practically all civilized countries.

After certain inquiry had been made by such means, the material gathered was worked up with the author's own notes and a draft submitted to a number of confreres, who made critical remarks as to the material therein contained, necessitating corrections and additions in order that the subject might be authoritatively presented.

A few correspondents, for reasons evidently connected with their own appointments, begged to be excused from participation in a joint article, as was the original intention, and thus their names are not herein quoted. Some of them expressed the fear that the necessarily diverse views of men working in such different surroundings and scattered over the world, could not be harmoniously collated in one article.<sup>1</sup>

The majority agreed with most of the criticisms and suggestions, and some with all, most of them giving additional ideas noted with their names. Wicherkiewicz, Cracow, says that it is a happy idea. Casey A. Wood, Chicago, and Hiram Woods, Baltimore, say that such an inquiry or statement may do a great deal of good, but that harsh words and antagonism may perhaps be expected by the author who shoulders such a responsible position. F. Maynard, Calcutta, says that it cannot serve a useful purpose.

A soldier who criticises the army, an official who finds fault in a department, or one who points out the errors and defects of a system of which he is a part will not lack criticism, vilification, and implications of base motives by some at least of his colleagues, for "there are those whom it is hard to move."<sup>2</sup> Therefore, as the writer has had some twenty years' experience in such positions, has been a critical observer of many such institutions both at home and abroad, and as he at present does not hold any such relations; except where otherwise quoted, the reader will ascribe to him the responsibility of these comments, remembering that some of the authorities do not accept the whole of the revised article even as it is here printed.

The criticisms contended for are general in their application, and local conditions must modify and govern them in all instances. What is true in American cities is not necessarily true in European cities, and *vice versa*, and criticisms intended in one country (herein mostly America) may not equally apply to all others.<sup>3</sup>

Some of the suggestions herein made may be looked upon as Utopian.<sup>4</sup> Some of our colleagues do not think that the criticisms

<sup>1</sup> Casey A. Wood, Chicago; F. Maynard, Calcutta; Henry R. Swanzy, Dublin.

<sup>2</sup> Marcel Danis, Brussels.

<sup>3</sup> Casey A. Wood, Chicago; Hiram Woods, Baltimore; Fredk. R. Cheney, Boston; J. Bistis, Athens.

<sup>4</sup> H. R. Swanzy, Dublin.

apply in their localities,<sup>5</sup> but these particular teachers have institutions and clinics which are eminently noted as the Mecca of ophthalmic students and only in minor details can any criticisms be made. Other correspondents, while agreeing with these contentions, do not care to be quoted, owing to their personal relations with certain institutions of which they well know the failings. Practically all of the correspondents accept the majority of the suggestions originally submitted for criticism.

Thus this essay may be looked upon as an editorial compilation, the assumed author thereof being the translator of what may be esteemed a matter of world-wide observation and cosmopolitan comment. We believe that our contentions are sufficiently well subserved without going into personalities and distinctions of institutions or localities, and no particular men or institutions are herewith noted. The manifest excellencies of many institutions, their good equipment, and the high quality of their teaching is borne in mind.

The necessity for the existence of charitable institutions for the relief of the diseases of the poor is evident, especially in some countries.<sup>6</sup> (1) For charity's sake; (2) on account of the economic importance of returning an otherwise able member of society to his work and thereby relieving him and his dependents from the necessity of public support; (3) the manifest need for training of students and the greater opportunity for perfection of technique that is obtained by contact of the surgeon and the teacher with much larger numbers of physically afflicted than could ever be afforded by the necessary limitations of private practice. Be this as it may, there are large communities which are not blessed with or afflicted by (the term depending upon the point of view) such eleemosynary institutions as free infirmaries, owing to the class of inhabitants and to the objections of their physicians to the pauperization of the community by establishment of free institutions which are not there needed.

The establishment of public hospitals and dispensaries should depend upon the environment: (1) Of most importance being their economic value and relations. If the city be the centre of a manufacturing community where accidents are common, or where many inhabitants are so poorly paid as to be unable to afford even a portion of the ordinary physician's fee, there is some excuse therefor, as the unproductive man may be returned to his work, the load of his support and that of his family lifted from the State, and actual economic charity thereby dispensed, and yet, as M. Uribe y Troncoso remarks, but Americans will not agree with him,

<sup>5</sup> F. Cheney, Boston; L. Webster Fox, Philadelphia; Henry Dickson Bruns, New Orleans; Hanford McKee, Montreal; Ernst Fuchs, Vienna; H. R. Swanzey, Dublin; Julius Fejer, Budapest; A. Maitland Ramsay, Glasgow.

<sup>6</sup> M. Uribe y Troncoso.



"some middle-class people who cannot afford the professor's fee will consult him in the free clinics," but middle classes are fully able to pay the usual oculists' fee, though some of them go to free clinics under false pretences, as is also remarked in my correspondence with Adolf Alt Wicherkiewicz and Da Gama Pinto, and is a notorious practice in some of our large American cities. (2) If there be in the city a body of students who be benefited by the sight, study, and handling of such cases another excuse is thereby granted. (3) Another reasonable excuse is that local physicians, by reason of their contact with large numbers of the afflicted, may increase their knowledge. The latter, however, in many instances is improperly applied, owing to the ambition of self-appointed members of the medical fraternity to style themselves "professor" and thereby in their own opinion elevate their standing in the community and increase their gains by the evident advertisement above that of simple members in the medical fraternity. (This criticism should be practically confined to certain institutions in America.) In some localities, however, there is ample room and a crying need for the establishment of additional professorships and charitable institutions.<sup>7</sup>

The position of the buildings intended for such purposes should be within reasonable walking or cheap transportation distance of the localities in which the poorer classes live and work. This requirement is generally well met.

The architectural design, mechanical detail, and construction of the buildings in which this business is carried on may be inferior, imperfect, insanitary, and never in the first place intended for such purposes. Naturally this is owing to the financial condition of some institutions, they being supported in part by charity, in part by enforced or more or less unwillingly given contributions from members of the staff, and in a few cases by charges to patients. All such institutions should be subsidized by the city, State, or country in which they may be located, as they form important economic items in the body politic.

Here may be interposed the evident abuse of infirmary privileges and the admission without proper evidences of pauperization of patients<sup>8</sup> who are really able to pay a medical fee and who thus deprive the young doctor of the means of livelihood. The ambition for crowded clinics is a basis for this complaint, and it is to be blamed upon the civil authorities as well as the surgeon in charge. Certain institutions try to create a halo of glory by the great number of patients taken care of each year.<sup>9</sup> The cure for this is a certificate showing need of services and inability to pay from a physician.<sup>10</sup>

<sup>7</sup> M. Uribe y Troncoso, Mexico.

<sup>8</sup> A. Sulzer, Paris.

<sup>9</sup> Adolf Alt, St. Louis.

<sup>10</sup> Henry Dickson Bruns, New Orleans.

In order to deliver what is due the patient, whether or not he pays what it is worth or receives the services gratis, the best mentally and physically equipped men in our profession must work in sanitary surroundings with sufficient equipment, and must have properly qualified assistants, in order to enable them to use their brains and thereby their hands for the best advantage of the patients. No new institution of this character should be started without proper financial backing, without proper buildings, complete in mechanical detail and construction, without proper equipment, and without proper lay management as well as medical attendance.

The organization of an eleemosynary institution should be in the hands of those who provide the funds; the power should be in a board of laymen whose business it will be to secure and apply the necessary moneys for the buildings and subsequent care of the institution. The decision of all matters of policy should rest with this lay board. "*Securus judicat orbis.*" The position of the medical man in the running of such an institution should be advisory only.

Time was when hospital directors and trustees shared the awe of the ordinary patient for the physician, and thought that, like the king, the medical man could do no wrong. After experience in organization and in the routine of hospital management it is found that, strange as it may seem, and vehemently as it has been denied, the physician as an officer may be governed by the most petty motives, by jealousy, greed, and envy, and by conceit and lack of sincerity.<sup>11</sup> Self-control and broad-mindedness should be attributes of the specialists in charge, and the door should always be open for personal animosity to go out.<sup>12</sup>

Directors and trustees have learned that the judgments of medical men and their confreres are to be taken *cum grano salis*, and that in any suggestion there are apt to be concealed personal, professional, or tactical motives. Therefore those who provide the funds should say how these institutions should be run. Lay boards of intelligent, capable, and upright business men know the aims and needs of the sick poor as well as physicians, and have no personal jealousies to keep them from attending to these needs in the right way. There should be an advisory medical staff before whom only should be brought up matters connected with sanitation, medical, and surgical therapeutics, and with the appointment of their confreres, assistants, and nursing staff,<sup>13</sup> as in Italy.

It is no exaggeration to say that the numbers of patients appearing daily before our larger institutions for diseases of the eye,

<sup>11</sup> Percy Fridenberg, New York.

<sup>12</sup> M. Wicherkiewicz, Cracow.

<sup>13</sup> Percy Fridenberg, New York. M. Cirincione, Rome.

ear, nose, and throat require staffs of at least double the number that are now serving them. The addition of new clinics, as well as increase of the number of surgeons and even of assistants, would afford relief,<sup>14</sup> but is opposed by those already in position. This is the tendency from time immemorial in close corporations, guilds, and similar bodies in all walks of life.

It is impossible to expect help from within. Protest from the ranks is "mutiny," from equals "perfidy," from laymen "imper-tinence." Evils are recognized by many on the inside who fear to lose favor with the powers that be if they suggest that there is anything short of perfection in the "best of all possible" institutions. When such is called to their attention the reformer is advised "not to stir up trouble; let somebody else do it; keep quiet; don't be known as a reformer; don't get disliked; or to get out."

Those who suffer the evils, namely, the poor, "have no right" to cry aloud, for they are "getting something for nothing." Those who have the power to abolish them are not aware of the conditions. Therefore, under such circumstances, the correction of such evils not being looked for from within, the authorities should have their attention called to them—as in all large clubs and social institutions—by the complaint box, one for the patients and another for the staff; an officer should be appointed to care for these evils, and to bring any that cannot be immediately corrected to the board of directors.

Some of the evils in the personnel are the inattention to duties of the nominal heads of the staff, the overcrowding of the clinics, the insufficient service, and small number of assistants.

In the dispensary there is frequently only one clerk in a poorly equipped corner who attends to perhaps two or three dozen or a score or so of patients. One or two assistants, not at all experienced in routine, refract 20 or 30 cases or more in the course of an hour. Even skilled oculists in private practice, with the good equipment of their own office, with skilled assistance of a nurse, and what is more important, a frame of mind necessary for the performance of this work, find it impossible to handle a dozen refraction cases in a day.

The assistants in our eye dispensaries have, as a rule, little or no practical training. They have to be trained by those next in rank, their seniors, who are already kept pretty busy with their duties. The result is desultory, imperfect, hurried, and consequently slovenly work, inevitable and not to be laid at the door of the individual unless it be the top rank man.

The head surgeon is really responsible for these evils, whose pride of office and position, or whose selfishness or professional jealousies keep down the number of positions to be filled by men

<sup>14</sup> M. Uribe y Troncoso, Mexico.

of equal rank and hence of supposedly equal capability, who overloads his own clinic, runs up the number of operations performed in his service, and saps his clinical assistants with routine work.

Apropos to this condition may be cited the fact that the pathologist of the staff is so, as a rule, only in name. This should be a paid position, and he should have a properly equipped laboratory in which to work. He should be in attendance at the clinic at its regular sessions, and not put his sole attention upon the mounting of microscopic specimens, but make routine examination of conjunctival secretions as well as pay attention to tumors or other interesting scientific work. A properly paid man should be employed to administer general anesthetics.<sup>15</sup> An official optician is a requirement in very large clinics, but even here it becomes a question whether a rota should be kept and revised frequently of competent and honest opticians, all working to a fair but not exorbitant charge.<sup>16</sup>

The institutional jog-trot now tends to discouragement of initiative and individual enthusiasm in the assistants. Insufficient attention is paid to the refraction work and to the commoner diseases of the eye, and only when some unusual case comes is interest displayed.

Many of the surgeons and assistants are unable to communicate intelligently with patients of foreign nationalities. An interpreter in our larger clinics and hospitals should be as familiar an officer as in the courts.<sup>17</sup> Such a person would have plenty to do and would save much valuable time, besides making it possible to get information, the lack of which in some cases obscures the diagnosis and to a certain extent cripples the treatment and consequent results. He would be of great aid in establishment of communication between the physician and patient, which must be the basis for all effective treatment. By the means of the interpreter clear directions could be given to patients and the time of the chief of staff thereby saved.

The patients themselves could be directly instructed not only individually, but collectively, by placards on the walls, telling them how to bathe the eyes, apply salves, how to take medicines, the teaching of how to avoid spreading eye disease and the first aid to the injured, their dietary and regimen, could be effectively communicated by such wall signs. Printed slips with clear, terse directions could be given with the first bottle, telling just how the contents should be used,<sup>18</sup> but among the ignorant this only does not suffice and the patients must be individually instructed.<sup>19</sup>

<sup>15</sup> Sydney Stephenson, London. A. Maitland Ramsay, Glasgow.

<sup>16</sup> Ibid.

<sup>18</sup> Ibid.

<sup>17</sup> Percy Fridenberg, New York.

<sup>19</sup> A. Sulzer, Paris.

In but few clinics is the clerical work sufficiently accurate. The work could be more advantageously done, not only for the patient, but for ophthalmic science in general, by special clerks to take the case histories. This might be the first position in which the aspiring assistant may be placed, progressing thence to the refraction room, thence to that of clinical assistant, and thence to that of assistant teacher.

We come now to the question of fees for treatment, medication, and appliances. Should or should not the individual "charity" patient be charged some small sum for his medicines, for his glasses, and for his appliances? A few persons apply to public infirmaries and yet retain sufficient self respect not to allow themselves to be wholly pauperized. Where the institution is not fully supported by the State or by some organization a contribution box should be in the waiting room, another in the refraction room, and another at the pharmacy. It is penny-wise-pound-foolish to require these patients to pay anything direct. These institutions should be supported by public and private contributions, not directly by fixed fees to the persons whom they are intended to help. Continental European clinics are in some instances conducted by a professor and supported by the State, the polikliniks by private docents and supported by benevolent societies.<sup>20</sup> Medicine should be furnished free. A fund should be established for the dispensing of lenses and frames, as well as for apparatus. No gold or gold-filled fittings should be given out. Medicines, glasses, and apparatus should be given in the simplest and cheapest form in which they will do the most good.

In regard to the medicines, eye drops should not be furnished in a corked flask—the eye dropper should be a part of the bottle. Salves should not be given in jars or wooden flasks, they should be in tubes. General medicines should be furnished in new and clean bottles. Certain medicinal foods, as the various infant and malted foods, should be dispensed. A special milkman, iceman, grocer, and butcher should be unofficially connected with the institution, his goods and his prices to be frequently supervised by the authorities. Favoritism of certain tradesmen (as insurance companies in Europe) should not be tolerated.<sup>21</sup>

Stress is now laid on the admission of operative cases to the hospital wards. There is a craze for cataracts, despite the small proportion of these cases in America, where the climate and methods of life are not conducive to this affection, and where it furnishes but a modicum of the operative cases. There is always room for one more operative case in the hospital, but rarely for those requiring constitutional treatment. It stands to reason that some serious affections, such as acute iritis, can be taken care of in the

<sup>20</sup> Julius Fejer, Budapest.

<sup>21</sup> A. Sulzer, Paris.

out-patient department. The cases most in need of bedside attention are serious accidents or those in which the eye affection requires constant rest in bed, or where severe constitutional disease effects the ocular disturbances. In the first category we have penetrating injuries of the eyes; in fact, all serious injuries in which there is a possibility of preserving the organ with useful vision. Exceptions should be made, however, in those eyes which are beyond all hope of recovery, and can just as well be attended to at the patient's house until they are in condition for enucleation. Acute glaucoma, cataract, and other serious affections demanding operation, and especially those for which a general anesthetic is needed, are, of course, hospital cases. The medical cases which need hospital treatment, as distinguished from operative, are those with accompanying cardiac, vascular, renal, or gastro-intestinal diseases with other complications. These are the ones which are now denied hospital admission, treated with some placebo, and kept on the go to the clinic week after week instead of being placed under observation and systematic, thorough treatment.

No undergraduate nurses should be employed in an eye hospital. They should be selected from capable graduates of general hospitals and be above the mental calibre of the ordinary servant girl, to which class so many of the applicants for the position of nurse belong. They should receive ward training and instruction in the clinics in the ordinary methods of eye treatment and special procedures. This is only done in a slipshod manner in most institutions. The lectures delivered to the nurses are likewise, as a rule, only of the most perfunctory character, although notable exceptions may be found in some of the larger ophthalmic institutions. The present discipline of the nurses does not leave much to be desired; it all depends upon the class from which they are taken and upon the wise rulings of a capable superintendent.

The house staff should be selected from the graduate students who have completed courses of lectures. No undergraduates in medicine should assist at clinics, prescribe medicines or lenses, do operations or refraction work, or under any circumstances give instruction in a post-graduate hospital. In some countries<sup>22</sup> the small recompense held out to medical men on account of poverty of the inhabitants renders it difficult to get first class men as assistants and then too the hide-bound and medieval character of the people does not permit proper social position of the medical profession. Trouble also develops from these characteristics in the management of hospitals and eleemosynary and teaching institutions.<sup>23</sup>

The course of training for special work should not only include ophthalmic operations and treatment of hospital cases, but should

<sup>22</sup> Da Gama Pinto, Lisbon.

<sup>23</sup> Ibid.

pay particular attention to refraction work, diagnostic methods, such as bacteriological examination of secretions, recognition of tubercle, diphtheria, of foreign bodies by the x-rays, and a working knowledge of the methods of localization. The pathology of the eye, immunization theories, and the principles of animal experiments, at least to the extent for which they are required for diagnosis, as in inoculation of supposed tuberculosis and the study of microorganisms. The principles of electrical treatment are not taught in a satisfactory manner in any of our institutions. Most undergraduates are as unfamiliar with electricity as is the high school student. The practical application of faradism, galvanism, and the high frequency currents is a blank page to them. Hydrotherapy and hot air treatment is sadly neglected.

The equipment of some eye hospitals and infirmaries is certainly not what should be expected. In the clinics even the test lens cases are incomplete, being used on different days by the staffs of various clinics, and are often dirty and in disorder. They should be kept arranged by the nurse, cleaned by phenol solutions or alcohol,<sup>24</sup> and the trial frames sterilized and some system of supervision exercised.

Diagnostic apparatus should be of the latest model instead of, as is often the case, being old or in bad repair. The test cards and types are frequently dirty and no attention is paid to proper lighting. This is readily obviated by using transilluminated opaque glass test charts. The treatment cases used at the clinics are seldom in good condition; the medicines in the bottles are not renewed until they have been used up; the droppers are used from one patient to another, offering ample opportunity for infection, particularly of trachoma. Sterilization of instruments, eye droppers, etc., is essential.<sup>25</sup> The same may be said of utensils, such as jars, which are passed from one patient to another without proper sterilization. Segregation of the infective cases, as conjunctivitis, ulcer of the cornea, panophthalmitis, and trachoma, should be made in special rooms or wards, and in larger institutions a children's ward is essential.<sup>26</sup> In these rooms special applications and instruments should be kept.

Almost all institutions having clinics for the treatment of special forms of disease, advertise instruction to practitioners of medicine in the corresponding specialties. These courses are supposed to be limited to graduates in medicine. In a few of these institutions this instruction is not at all in accordance with the prospectus and advertisement, neither in the help offered to prospective students nor by the promises given in return for the fees; these promises referring as much to the spirit as to the scope and detail of the teaching. Graduates from small colleges in other cities, many of

<sup>24</sup> M. Wicherkiewicz, Cracow.

<sup>25</sup> Marcel Dapin, Brussels.

<sup>26</sup> Ibid.

them practitioners of long standing, come from small towns or rural districts attracted by the names of eminent clinicians and the reputation of skilled operators to learn from them the secret of their success and to acquire under their supervision a little of that excellence to take back to their own patients and apply to their own practice.

Every institution giving post-graduate instruction prints a long list of such luminaries as star attractions of their course. What are the facts of the case? And what do the special students get? Many of the stars, he finds, are connected with other institutions which are mainly or exclusively didactic or pedagogic, and to these the star devotes most or all of his time, neglecting or absolutely denying any duties or responsibilities in the clinical school other than having his name appear in print. Some of them reduce their presence in the hospital to one weekly visit of hardly an hour, and they are penetrated with a deaf hostility to those who give a reasonable part of their time and activity.<sup>27</sup> Others are opposed to the school altogether, but have allowed their names to be printed on the prospectus—as no one objects to being advertised as long as it is done ethically. These teachers shun their clinical students, refuse them admission to their clinics, and forbid their assistants to teach them unless they pay a special fee therefor. The bulk of the teaching, therefore, devolves upon the assistant teachers, many of whom are efficient and ambitious, with enthusiasm for demonstration and a gift for imparting knowledge. They come into closer contact with the post-graduate, as does the tutor at college or the privat docent abroad, and from these men much can be learned. Their disadvantages, however, are many. The routine of clinical work takes up a great deal of their time, and the work of the clinic suffers if they spend much time in teaching. Of course, with adequate assistance both functions could be carried out perfectly well, but this would require a larger staff and new heads of departments, and we have seen where the opposition to this reform is deeply rooted.

Instruction in refraction, diagnosis, pathology, general operative technique, and the details of after-treatment, as well as clinical diseases and special courses in the physiology of vision, could well be given by such assistants, provided that they showed they were fitted for these duties, the surgeons limiting themselves to operative surgery of the eye and clinical ophthalmology. The turning out of poorly trained and hence incompetent oculists by some poor graduate schools is one of the results of slipshod instruction.<sup>28</sup> But in the writer's personal experience such self-styled specialists are premature deliveries of even the best institutions—self-inflicted abortions in fact, caused by systemic disease in the embryo, and

<sup>27</sup> A Sulzer, Paris.

<sup>28</sup> Hiram Woods, Baltimore.



are largely of the class of men who obtain their special education by a few weeks or months of superficial observation of European clinics—some of these aspirants not even having a smattering of the foreign language used by the professor.

An ideal school, in addition to the usual medical and operative courses, would offer instruction in the hygiene of vision, ocular dietetics, prophylaxis of infection, prophylaxis of injury to the eyes, the prevention of blindness, as well as the management, training, occupation, and care of the blind; a study of occupational eye diseases, of eye injuries connected with the various trades, together with visits to the various manufactories and institutions, the examination of machinery where accidents are liable to occur, study of the management of these factories, workshops, and of mine work should be given. The economic question of blindness and its relation to the State, charities, and insurance, might be considered. Instruction of special nature for oculists should be (in addition to diseases and operations) the study of those affections which are the effect of or are necessitated by the environment and general conditions, the study of ophthalmic and optical questions, the use of special apparatus, study of models of optical instruments, investigation of the color sense, and other points in the physiology and pathology of vision. Electrotherapeutics is generally sadly neglected. The specialists in electrotherapeutics have ordinarily a holy terror of the eye, and will not give sufficient dosage to be therapeutically efficient.<sup>29</sup> Each oculist should be well versed in electrotherapeutics and radiology so that he may at least personally direct their application.

The scope of instruction, or rather its object, might be widened to include laymen who devote themselves to work in which diseased eyes and poor vision are factors. Settlement workers, teachers, officials in reformatories and charitable institutions might take such courses to the advantage of those committed to their care.

We hope that the educational value of this article will be considered by the reader to outweigh individual idiosyncrasy and to balance any Utopian ideas that may be herewith promulgated. We recognize, as any fair observer must, what inestimable good is being done, how much is being accomplished, and how much the good outweighs the bad. There is, however, much room for improvement in our eye dispensaries and teaching institutions, and much might be added to the ultimate results and savings. It is with a recognition of these possibilities and of the very evident need of reform in institutions, and with the still more evident possibility of bringing about such reform, that we endeavor to call attention to the sins of omission and commission, and to come nearer the perfection which could be reached were the effort made by those most directly interested.

<sup>29</sup> A. Sulzer, Paris.

THE TREATMENT OF LOCOMOTOR ATAXIA.<sup>1</sup>

BY EDWARD LIVINGSTON HUNT, M.D.,

ASSOCIATE CONSULTING NEUROLOGIST, ST. LUKE'S HOSPITAL, NEW YORK.

To outline a definite plan for the treatment of locomotor ataxia is difficult. To lay down hard and fast rules is impracticable. To treat every patient alike is not possible. Conditions are complex and symptoms numerous; in each case there has to be considered the treatment not only of the disease but also of the individual. It is true that the earlier a patient comes under treatment the better will be the results; it is true that the more persistently he remains under treatment the more lasting will be the results; it is true that the more negligent he is of treatment the more disastrous will be the results.

Every case of tabes should have both a physical and laboratory examination. In every case there should be made an ophthalmoscopic examination; in every case there should be made a Wassermann test. In ordering a Wassermann test it should always be remembered that if the blood is taken too soon after the administration of either mercury or arsenic the result will be valueless. Mercury and arsenic for a period of twelve weeks after their administration render the Wassermann test negative.

Locomotor ataxia is a parasyphilitic disease. In its treatment, therefore, it is of importance to weigh the value of salvarsan and mercury. Salvarsan does little good; instances have been reported where its administration has aided, but these cases have been few and early. Nonne thinks that its administration has, for a time at least, relieved some of the symptoms. There has been no real definite proof that in locomotor ataxia any marked or permanent help has followed the use of salvarsan. Such good as has resulted has been of a transient nature, and decidedly questionable. On the other hand, instances have been chronicled where its use has inaugurated an optic neuritis and hastened an optic atrophy. It should not be given if arsenic has been recently administered.

Mercury is of benefit. To my mind its use is indicated in every disease where the etiology has been proved to be syphilitic. In tabes the contraindications to its use are a beginning optic-nerve atrophy, well advanced cases, dyspeptic and anemic cases, and those which show an intolerance or those which have had a great deal of mercury. It is best administered by the hypodermic method, the next best method is by inunction, and the poorest way to administer mercury is by the mouth. The fundus should be examined; if there is any indication of an involvement of the optic nerve neither salvarsan nor mercury should be given.

<sup>1</sup> Read before the Medical Society of the State of New York, April 16, 1912, at Albany, N. Y.

The question as to whether or not the patient is in need of mercurial treatment is one difficult to decide. The best guides are the general condition of the patient, the index afforded by the Wassermann test, and the clinical evidence as to whether or not the tabetic process is arrested.

The treatment of the seat of the disease consists of such measures as may be directed toward improving the local nutrition of the cord. These consist (1) of counterirritation, as galvanism, hot and cold applications, and especially the cautery; (2) of measures directed toward stretching the cord. Formerly this was accomplished by having these patients hang from a parallel bar, but more recently there has been adopted a safer and more reliable method, namely, that of flexing the trunk upon the extended legs while the patient is on the floor in a sitting posture.

The treatment of the symptoms can best be considered in the order of their importance and frequency. The first, the most common, and the most distressing symptom of tabes is the pain. It occurs in 88 per cent. of the cases. First, simple external remedies should be tried, such as hot-water bags, the application of sand bags, ironing, ices, iodine, mustard, and plunging the leg in alternating hot and cold baths. Dry cups, the cautery, chloroform liniment, firm bandaging, vibration, massage, and faradization can and should be tried. If in spite of these remedies the pains still persist or tend to become worse the patient should be put to bed and resort had to internal remedies. For this purpose a host of drugs have been employed. One may choose from aspirin, antikamnia, pyramidon, antipyrin, codeine, salpyrin, and even sodium salicylate. A French method, which consists of injecting a weak solution of cocaine into the subarachnoid space should also be mentioned. It is neither practical nor free from danger. Finally, there is the hypodermic of morphine. This should only be given by a physician, and then as a last resort. If, however, nothing else relieves the patient it should be given unhesitatingly. It is a curious, but nonetheless true, fact that the particular remedy which will at one time relieve the attack of pain will at another time utterly fail. Rest is a powerful aid, and these patients are greatly benefited by prolonged periods of rest in bed and by nourishing food.

The second most common symptom of tabes is disturbances of the bladder. These occur in 80 per cent. of the cases. Here there are few drugs which can aid us. Strychnine to give tone to the bladder wall, ergot, and urotropin if cystitis has developed. Much can be done, however, by careful attention to the bladder. The patient should be taught to empty the bladder at fixed and frequent intervals, and, if necessary, bladder washings given. The catheter should be kept as a last resort. The passing of sounds, faradizations to the perineum, and even the stimulating of the urethra by local

applications of nitrate of silver sometimes help. This aid may only be of a psychic nature, but nonetheless I have seen it help, and consider it justifiable.

Ataxia of the legs occurs in 75 per cent. of cases. Here treatment gives brilliant results. The patient can be taught the Fraenkel exercises. These consist of a series of mild gymnastics, performed at first in bed, later when standing, and finally when walking. The object is to reëducate the legs: first to stand, next to step, and then to walk. The patient should do these exercises without the aid of a stick or his eyes. Persistency is required; a daily course of these exercises should be followed for fifteen minutes in the morning and again in the afternoon. The physician should carefully observe the patient, as the latter is apt to overdo and tire himself. The tabetic is in no way capable of judging of his own capacity, a point which cannot be too strongly emphasized. The Fraenkel exercises are numerous, but space is lacking to go into them here in detail. These exercises can also be applied to the hands; precise and delicate motions can be practised, which will give very remarkable results.

It is important that these patients learn to walk without the aid of their eyes. Let me emphasize that women tabetics are troubled very little with ataxia. This may be due to their skirts. Also that those ataxia cases which become blind, invariably improve in so far as their walking is concerned. These two instances call our attention to the importance of having the ataxia patient walk with his legs and not with his eyes.

The diminution of the sexual desire is unfortunately beyond the aid of the medical man. Tonics and aphrodisiacs can be tried, but usually accomplish but little. Damiana, strychnine, and yohimbin give the best results, but even they prove unavailing.

Perforating ulcer of the foot is an unusual complication. It occurs in 5 per cent. of the cases. The treatment is rest in bed, protection in the form of a local application, and finally stretching of the posterior tibial nerve.

The ocular palsies, involving the second, third, and sixth nerves, occur in about 10 per cent. of the cases. The treatment of these is unsatisfactory. For the diplopia a shaded glass can be worn. I have a patient who suffers from this condition, and to do away with it wears a pair of eyeglasses in one of which the glass is opaque. In cases where there is sixth-nerve paralysis, resort can be had to constant exercises, consisting of training and reëducating those muscles.

Ptosis is always a distressing symptom. It fortunately is not of common occurrence, and frequently yields to antisyphilitic remedies. If permanent, surgical measures may have to be considered. A tuck can be taken which will keep the lid up, but will, of course, not affect the accompanying double vision. Electricity here is of no use.

The treatment for the optic neuritis and for optic nerve atrophy has so far proved unavailing. Strychnine in daily doses may delay the atrophy. Mercury should be stopped.

The joint deformities are difficult to treat. Mechanical appliances sometimes aid, but even amputation may have to be considered. These joint complications, however, do best if let alone.

The crises which occur in tabes are varied and numerous. Contrary to general opinion, they are of unusual occurrence, as one meets with a crisis in only about 6 per cent. of the cases. They are best classified in accordance with the several viscera. The most important for the therapist and the one which is most commonly encountered is the gastric crisis. The treatment of the gastric crisis is either medical or surgical. Medical treatment is the least radical and the most practical. The most serviceable drugs are cerium oxalate in 5-grain doses every half-hour, minute doses of strychnine, antipyrin in frequent and small doses, chloral hydrate, cannabis indica, and some of the alkaloids of opium, as codein and dionin. Powdered opium itself can be administered, first in the form of suppositories and later hypodermically. Methylene blue in 1-grain doses has been tried. Oppenheim speaks of injections of cocaine into the epidural and subarachnoid spaces of the spinal canal. Levy and Pope have added to these injections alcohol and stovain. Simple lumbar puncture has been done with but scant results. These latter methods are, however, far too radical and far too impractical to warrant serious consideration in every-day practice. A patient who is subject to gastric crises should have a series of simple and harmless remedies, which he can use when the crisis occurs. If, after repeated attempts there is no abatement, hypodermics of morphine are indicated and should unhesitatingly be given. The hypodermic of morphine should only be given when all reasonable remedies have failed and when the patient has reached a point where decided inroads are being made upon his reserve strength and vitality. This means that every effort should be put forth between the attacks to build up the patient and to feed him so that he will be prepared and ready to withstand an attack of vomiting. It is this intercurrent treatment which is the keynote of the treatment of the gastric crisis.

The surgical treatment, which consists of dividing the posterior nerve roots, has been recently written of and tried by some. Personally I have had no experience with it, and except as a last resort should hardly be inclined to advocate it. A patient with tabes is to my mind not a fit subject for a serious operation, provided that such operation can be avoided.

The laryngeal crises can best be helped by sprays of menthol, and as a last resort cocaine.

The rectal crises can be relieved by suppositories and fomenta-

tions. The crises of the other viscera have to be met by the administration of many and varied local remedies as well as by opium. In tabes morphine is a powerful, but a dangerous aid—one to be used with great judgment, but in supreme moments with no hesitation.

The treatment of the mental condition of the patient is important. The tabetic is peculiarly susceptible to suggestion, and is constantly seeking new remedies and outside aid. His condition is ever before him. He is sensitive, easily depressed, and easily exhilarated. Hope springs eternal—undoubtedly a wise provision of nature, and one which should be encouraged. A change of treatment, a new remedy, a new suggestion, however trivial, will often start one of these unfortunates upon a new lease of life. The physician should bear this in mind and never relax in his efforts to make new suggestions and to stimulate hope.

The treatment of the physical condition of the tabetic is all important: The disease is characterized by sudden and unexpected crises and exacerbations. Constant efforts should therefore be made to improve the general health and to fortify the strength. A reserve of energy and force is of great value. The degree of anemia, the blood pressure, and the weight should be closely watched. A tabetic who loses weight is not doing well; a tabetic who gains weight is doing well. A simple but nutritious diet helps; one abounding in fats helps more. Cream, butter, bacon, marrow, and oils are indicated. Baths aid, warm baths especially. They serve to quiet these patients, to relieve the pain, and to improve the general nutrition. Carbonic acid baths are of service. Spinal douches, if not too violent, are useful. General tonics—iron, strychnine, and especially arsenic—are from time to time of great value. If much emaciated, cod-liver oil is indicated; and if the stomach is disturbed, *nux vomica* may be useful. Constant and unremitting attention must be given to the bowels. One of the great horrors of the disease is the obstinate constipation. Laxatives, plenty of fluids, fruits, and enemas must be used.

So far as climate is concerned, the tabetic does better in summer than winter, and therefore in a warm, dry atmosphere. These patients move about with so great difficulty that few if any obtain sufficient air, a factor which is not sufficiently recognized and one which is of great importance. A change of environment will often prove beneficial. A month spent at Lamalou les Bains in France is very helpful.

Rest is a wonderful aid. Many of these sufferers fail to do well under every condition, but let them spend two or three days in bed and the improvement is remarkable. Rest in bed aids them physically and aids them mentally. Massage is serviceable to them, especially at the beginning. They should be constantly cautioned against physical strains and exhausting effort.

Finally, the treatment of tabes is one in which there should be constant supervision. The greatest attention should be devoted to details. Drugs should be used as sparingly as possible. Air, rest, hydrotherapy, and fattening food should be tried, while the physician should adopt a never-failing attitude of hope and encouragement.

## TUBERCULIN THERAPY IN SURGICAL TUBERCULOSIS.

BY THOMAS WOOD HASTINGS, M.D.,

PROFESSOR OF CLINICAL PATHOLOGY IN THE CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.

(Concluded from page 270, August, 1912.)

### PART V. TUBERCULIN CONTROLLED BY OPSONIC INDEX.

CONTROL BY OPSONIC INDEX. Wright<sup>102</sup> (1910) still claims that the opsonic index is of value in diagnosis, and for guidance in dosage in a certain class of cases. On the following pages of the same number of the *Lancet* (page 885) there is recorded a lengthy discussion by Latham, Hewlett, Walters, Warner, and Lawson, and, with the exception of Lawson and Wright, all conclude that a careful observation of clinical symptoms is more valuable than studies of the blood serum for a guide to dosage. Latham<sup>34</sup> and Leishman<sup>103</sup> believe that clinical observation forms a good guide for vaccine therapy.

MANAGEMENT OF DOSAGE. A dose of vaccine followed in twenty-four hours by a rise in temperature, or increase in fluctuation of temperature, or by exacerbation of symptoms, is too large. A dose producing no effect upon the temperature, and no change upon the symptoms, is too small. The proper dose is one which either lowers the temperature or is followed by a diminution in the fluctuation of temperature, and by improvement in the symptoms; and when the effect of the proper dose becomes less, the dose should be increased; but the dose which gives good results should be repeated. These rules apply also to tuberculin therapy.

Inman<sup>98</sup> states that it is essentially an individual treatment. There are three guides: (1) The general condition of the patient; symptoms, physical signs; (2) the temperature curve; (3) investigation of the serum. Each is valuable, but together each is more valuable.

Emery<sup>35</sup> states that the opsonic index affords no clue to the antibodies formed, and that the same benefits may be obtained by simpler methods. Control by the opsonic index, or any other method of serum examination seems unnecessary. Wright's<sup>102</sup>

results show that the length of treatment varied from two to thirty-nine months, a variation similar to that recorded by Sahli, Denys, Trudeau, who have controlled cases for years by careful

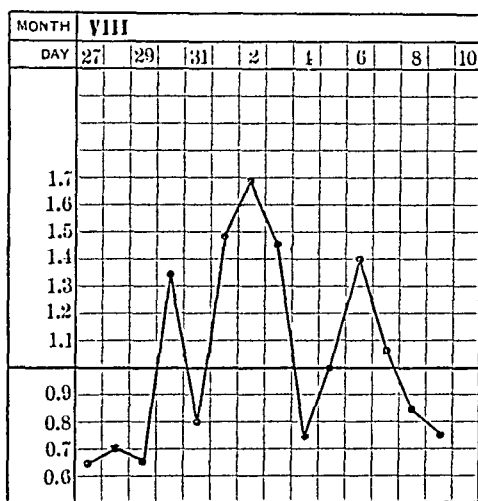


FIG. 5.—Opsonic index to tubercle bacillus. Incipient pulmonary tuberculosis.

observation of the clinical signs and symptoms. Such variations are so dependent upon the individual response at one time and another, and the opsonic index is so fluctuating in an individual

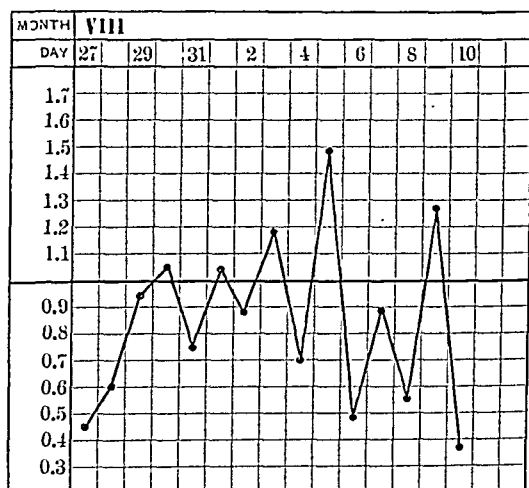


FIG. 6.—Opsonic index to tubercle bacillus. Case of advanced pulmonary tuberculosis.

invaded with tubercle (Figs. 5 and 6), as shown by Reyn and Kjer-Petersen,<sup>134</sup> Hastings,<sup>105</sup> and van der Weij,<sup>106</sup> and many others, that injections should be given *regardless of the index*,



provided the patient shows immediate tolerance and subsequent improvement (Fig. 7).

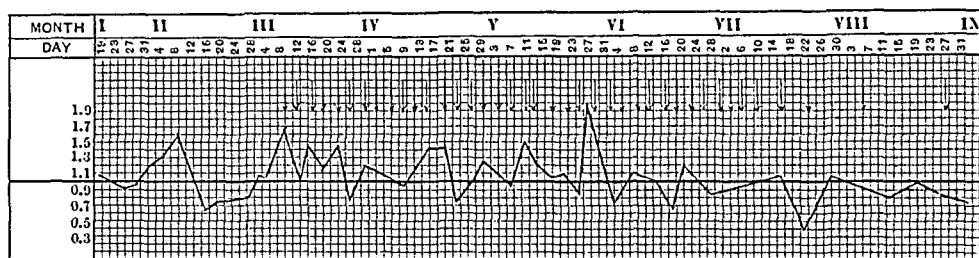


FIG. 7.—Opsonic index to tubercle bacillus. Cervical adenitis, tuberculous.

## PART VI. RECORDS OF INOCULATIONS.

The use of tuberculin for surgical cases is of later development than for pulmonary cases. Among the first reports are those of Petruschky<sup>4</sup> (1904), von Hippel,<sup>107</sup> Dörschlag,<sup>108</sup> Nourney,<sup>109</sup> Denys,<sup>12</sup> Heermann,<sup>110</sup> Wright,<sup>58</sup> Bulloch,<sup>111</sup> Kraemer,<sup>112</sup> Walker,<sup>113</sup> Köhler and Lenzmann,<sup>114</sup> and Birnbaum.<sup>115</sup> Wright<sup>58</sup> has recently given a table relating to surgical cases; but his experience does not equal that of Nathan Raw,<sup>116</sup> who is probably handling with tuberculin more cases of tuberculosis, pulmonary, and surgical, than any one other individual, and has had experience with gland, genito-urinary, peritoneal, bone, and pelvic (gynecological) infections.

**SURGICAL.** One finds scattered throughout the literature on pulmonary invasion isolated instances of a few case reports on surgical conditions (Petruschky, Denys, Klebs, Barney, Pottenger), and a few articles have appeared recently in this country by Hartwell and Streeter,<sup>117</sup> Thomas,<sup>118</sup> Winslow,<sup>119</sup> Peter,<sup>120</sup> Clark,<sup>121</sup> and Pottenger.<sup>122</sup>

This report covers the study in detail of over 174 cases. The cases are grouped according to the anatomical focus invaded as follows: (1) Larynx, 4 cases, 1 death; (2) glands (adenitis), cervical, 43; iliac, 2; 45 cases, 3 deaths; (3) eye and adnexa, 9 cases; (4) tongue (glossal), 1 case (with advanced pulmonary and cervical gland tuberculosis), 1 death; (5) skin (lupus), 3 cases; (6) bones and joints, orthopedic, 65 cases; (7) peritoneum, peritonitis, 5 cases, 2 deaths; (8) intestine, intestinal, 2 cases, 1 death; rectal, 4 cases; (9) adrenal glands, Addison's disease, 5 cases, 5 deaths; (10) genito-urinary tract, 31 cases, 1 death.

A summary of the above shows a total of 174 cases, 13 deaths; 6 cases with pulmonary involvement, 1 renal case with no involvement other than in genito-urinary tract, 5 cases of Addison's disease, and 1 case of general tuberculous adenitis.

**LARYNGEAL.** Tuberculosis of the larynx is classed, as a rule, under the respiratory and pulmonary invasion, and favorable reports have been made by Jurasz,<sup>123</sup> Pottenger<sup>122</sup> and Winslow.<sup>119</sup>

We have recorded 4 "open"\* cases, 3 of them complicating some other form of surgical tuberculosis, and improvement has been noted in all lesions in such cases. The total of cases to date treated or now under treatment is 7, and of these 1 only has died. Three cases which have been under treatment less than one year are not included in this report.

**GLANDULAR.** Results for gland invasion, in a small number of cases, were reported by Petruschky<sup>4</sup> in 1904, and Wright<sup>53</sup> in 1905. Denys,<sup>12</sup> in 1905, recorded and pictured the results of B. F. in the service of Sluyts, who treated 20 cases with tuberculin and by minor surgical methods, resulting in 20 cures which were slow in their course, but without radical operation.

Inoperable adenitis, "open" or "closed," responds readily to injections but a cure may require three years. Our cases are 45, 42 postoperative; 43 cervical, 2 with mediastinal and 2 with axillary involvement; 33 "closed" postoperative; 3 "closed," no operation; 7 "open" postoperative, and 2 inguinal "closed" postoperative.

Of the 43 cervical, 3 were complicated with renal or cystic or other genito-urinary involvement; 5 with pulmonary (2 deaths); 6 with ophthalmic involvement; 1 case died six weeks after cessation of treatment with symptoms of brain tumor and finally, of cerebral hemorrhage. Total deaths, 3.

In 2 cases, only possible recrudescences of the infection were noted, in 1 in the spine and in another possibly in the brain as a solitary tubercle. Abstracts of the histories of these 2 cases are inserted here.

**CASE I.**—Marjorie K., aged two years. Tuberculous cervical adenitis, two and one-half months duration; suppuration; two operations, with little improvement; temperature variable, usually three days out of the week to 102.5° F. in the late afternoon. Inoculations from February 19, 1910, to September 1, 1910 (six and one-quarter months); 30 inoculations; mixed vaccine, *Micrococcus aureus* and *pneumococcus* from May 10 to September 1, 1910 (19 inoculations); reported upon one year after apparent cure; recrudescence of tuberculous disease in spine.

One month after an attack of influenza, November, 1909, in Florence, the cervical glands in the right side began to enlarge. Operated upon in England, December 24, 1909. Profuse suppuration of wound continued and on January 20, a more thorough operation was done on right neck. Two open wounds persisted.

February 18, 1910. Adenoids and tonsils removed. Cultures from cervical wounds sterile.

\* For explanation of terms "open" and "closed" see page 262

Tuberculin injections begun February 19, 1910 (0.1 c.c. of 0.0000001); weight, 30 $\frac{1}{4}$  pounds.

March 8. Weight, 28 $\frac{1}{2}$  pounds. Otitis media left.

March 22. Micrococcus aureus from wound and left ear.

April 8. Nares and ears treated for infection. Conjunctivitis right eye, autogenous Micrococcus aureus vaccine (50,000,000).

April 20. Purulent conjunctivitis both eyes.

April 27. Weight, 29 pounds; temperature to 105° F., and a second acute middle ear infection. In cultures Micrococcus aureus and pneumococcus were found and a mixed vaccine was prepared. Tuberculin had been continued. Wounds healing.

May 15. Fifteenth inoculation (0.4 of 0.000001) of tuberculin. Mixed vaccine 25,000,000 pneumococcus, 75,000,000 Micrococcus aureus. Condition excellent.

May 25. Conjunctivitis recurred in both eyes.

June 11. Tuberculin injections had increased to 0.1 of 0.00001. Weight, 31 pounds. Tuberculin injections continued; vaccine injections discontinued. Patient removed to the country.

September 1. Condition excellent, apparently cured, and injections of tuberculin discontinued.

December 1. No recurrence in the glands and general health excellent. Seven months after last tuberculin injection symptoms of invasion of the spine and two months later Pott's disease well established.

CASE II.—Dr. W., aged thirty-eight years. Tuberculous adenitis, cervical, submental, axillary, mediastinal (?). Four years before coming under observation, right and left cervical glands enlarged, following an attack of tonsillitis; radical operations in May, 1906, and October, 1906; several minor operations up to and during 1908; improvement after surgical intervention temporary; hygienic treatment from 1906 to 1908; temperature quite regularly to 101° F. in the late afternoon. Tuberculin inoculations December 16, 1907, to August 19, 1908; from September 21, 1908, to December 14, 1908; from January 30, 1909, to August 17, 1909; from December 15, 1909, to January 30, 1911 (90 inoculations). Tetanus antitoxin August 19, 1908, serum-disease. Autogenous Micrococcus aureus vaccine from March 31, 1908, to May 26, 1908; from November 7, 1908, to August 2, 1909 (47 inoculations), under observation 3 $\frac{1}{2}$  months after last tuberculin inoculation January 30, 1911; under good hygienic surroundings from 1906 to 1911; death sudden following symptoms of brain tumor May 14, 1911; autopsy not permitted.

In 1903 there developed cervical bilateral adenitis following tonsillitis. Operation May, 1906, in the left posterior triangle and left axilla. Left cervical area was filled with purulent tissue and was curetted. Tubercle bacilli were found. Complete removal was impossible. In October, 1906, submental region left to right

and right cervical tissues were removed. "Recurrences" found later when wound dressings were removed, and right axilla was found involved. From June, 1907, to December, 1907, was at Saranac Lake. Previously had been living in Pittsfield, Massachusetts, and now resides there, undergoing the regular tuberculosis cure. Inoculations were begun December 16, 1907 (0.1 c.c. of 0.000001) at three or four day intervals.

January 8, 1908. Right neck opened and curetted.

January 15. Right neck again curetted; no inoculations were given for ten days after operation.

February 14. Marked improvement since January 26, and was given 0.5 c.c. of 0.000001. Slight general reactions followed the inoculations from December 16, 1907, to February 1, 1908.

April 14. *Micrococcus aureus* was isolated from cervical wound and an autogenous vaccine prepared and 200,000,000 to 400,000,000 given at five-day intervals. Tuberculin continued at three to four-day intervals (0.1 c.c. of 0.000005).

April 26. Marked general reaction after 0.2 c.c. of 0.000005.

July 11. Dosage reached 0.2 c.c. of 0.00001.

August 25. No tuberculin given until September 25, on account of "serum krankheit" following tetanus antitoxin on August 19.

September 21. Inoculations resumed (0.2 c.c. of 0.00001).

December 14. Episcleritis from *Micrococcus aureus* vaccine. Dosage reached 0.5 c.c. of 0.00001. No tuberculin or vaccine until January 30, 1909.

January 30, 1909. Weight, 160 pounds, a gain of 12 pounds. Wounds in left neck still discharging but much smaller. Inoculation of tuberculin 0.2 c.c. of 0.00001; *micrococcus* vaccine, 370,000,000.

April 27. Last vaccine April 27. Episcleritis recurred and promptly cleared up after withdrawal of vaccine.

June 20. Tuberculin omitted for two injections on account of possible "hypersensitiveness" (eyes). No improvement in episcleritis noted.

August 2. Vaccine stopped and episcleritis cleared in ten days. Pain in eyes twenty-four hours after *Micrococcus aureus* vaccine. Tuberculin reached 0.3 c.c. of 0.00005.

August 17. Weight, 166 pounds, a gain of 18 pounds. Tuberculin withdrawn. Sinus nearly closed.

November 19. Weight, 156 pounds. A loss of 10 pounds. Evening rise in temperature during last ten days, and asthenia. No tuberculin since August 17.

December 18. Tuberculin injections (0.1 c.c. of 0.0000001) again begun. Acquired immunity lasted three and one-half months.

December 24. After two tuberculin injections regained energy. Weight, 157 pounds.

1910. From January to March dosage increased to 0.4 c.c. of 0.000001, and gain in weight, 162 pounds, and marked improvement noted.

August 30. Weight, 173½ pounds. After an injection of 0.5 c.c. of 0.00005 a local reaction occurred.

October 10. In excellent health, weight, 175½ pounds, a gain of 27½ pounds. Given 0.8 c.c. of 0.00005 at intervals of ten days. Wound healed. Axillary glands small.

November 20. Given 0.5 c.c. of 0.0001; apparently well. Weight, 182 pounds, a gain of 34 pounds.

Last injection (0.5 c.c. of 0.0001) January 30, 1911. Five months after last injection of tuberculin indefinite symptoms suggesting cerebral involvement. At an interval of one week two attacks with headache, projectile vomiting, then apparent recovery. At the end of fourth week a similar attack with disturbance of vision, with apparent recovery at the end of ten days. No symptoms and general health good for three days then a sudden attack with explosive vomiting, slight headache, beginning optic neuritis, in both eyes (?) and death at the end of twelve hours with symptoms of cerebral hemorrhage (?).

Two full series of injections were given over a period of three and one-half years. The second series included injections of an autogenous *Micrococcus aureus* vaccine and of tuberculin.

CASE III.—Thomas C., aged thirty-seven years. Tuberculous adenitis, cervical, fifteen years' duration. The abstract of a third history is interesting mainly from the fact that recurrence appeared within six weeks from cessation of the tuberculin, and that recovery was complete, though slow, after an operation more radical than the two which had previously been performed.

Four and one-half years ago radical operation, right cervical region; seven months ago radical operation, left cervical region; recurrence in right lower anterior triangle of neck; temperature variable, with slight rise to 101° F. in the late afternoon; no complications, hygienic treatment thorough; advised against third operation. Tuberculin inoculations from April 30, 1907, to December 13, 1907 (34 inoculations).

December 15. A large tender lymph gland noted in the left axilla.

May 28. No tuberculin since May 13, enlarged gland in left axilla persists; no recurrence in the cervical regions.

June 20. Went abroad; operation on both axilla.

Cervical glands on the right side were noted enlarged in 1892; apparently quiescent until the fall of 1902, when they rapidly enlarged and a radical operation was done, the right cervical tissues from the parotid to the clavicle being removed. In October, 1906, the left cervical tissues were removed in the same manner.

April 25, 1907. Recurrence noted in the last few months on the right side, none on the left side; general condition is good; weight, 166 pounds, 11 pounds more than normal. Patient has recently been examined at Saranac Lake; fresh air, limitation of work, and tuberculin advised. Operation advised against by competent surgeons.

April 30. Patient was advised to construct a sleeping shack on the roof. Tuberculin inoculations begun, 0.2 c.c. of 0.000001; inoculations given twice a week, and gradually increased until September 14.

September 21. Inoculations had increased to 0.2 c.c. of 0.0001, interval between inoculations lengthened to one week. For the first time in several months the angle of the right jaw can be felt.

September 28. Following the inoculation of 0.3 c.c. of 0.0001 a moderate general reaction.

October 20. A moderate general reaction following 0.4 c.c. of 0.0001.

October 26. Enlarged gland noted in the left axilla, not tender. Following the reaction on October 20; dosage reduced to 0.3 c.c. of 0.00001.

November 26. Gland in left axilla decreased in size, slightly tender; patient feels much improved.

December 15. Forty-eight hours after 0.5 c.c. of 0.00001, the gland in the left axilla, was more painful and more tender, and the periglandular tissues considerably swollen; no constitutional symptoms; loss in weight of 13 pounds.

December 22. General condition much improved; patient has received no tuberculin since December 13; axillary glands much swollen. The pain and tenderness in the left side explained by the sudden appearance of a well-distributed herpes zoster.

May 28, 1908. The glands in the left axilla are still enlarged. No recurrence in the neck, and no tuberculin since December 13, 1907.

June 20. The patient went to Europe.

October. Temperature returned, and he was ill before landing on the Continent (axillary glands). Went to Austrian Tyrol, and there was in the hands of a sanitarium expert, who advised treatment with Beraneck's tuberculin. Did not accept advice, but went to Kocher, in Bern, who performed a most radical operation in the axillary region; febrile illness lasted several weeks; able to return home in the late summer, and has continued the out-door treatment and roof sleeping.

EYE AND ITS ADNEXA. - For tuberculosis of the eye and its adnexa, tuberculin was used by von Hippel<sup>107</sup> and by Dörschlag<sup>108</sup> prior to 1905. An excellent experimental study of such cases was made by Daels<sup>27</sup> in 1907, and articles dealing with the clinical results have come from Snell,<sup>124</sup> Brueckner,<sup>125</sup> Bull,<sup>126</sup> Darier,<sup>127</sup> Dor,<sup>128</sup>

Derby,<sup>129</sup> and Herrenschwand,<sup>130</sup> all of whom agree as to the beneficial results from tuberculin.

SUMMARY.—Of our 9 “closed” cases, the outcome is unknown in 3, the process was arrested in 1, and 5 were cured.

TUBERCULOSIS OF THE TONGUE. We have treated one “open” case, which was complicated with the presence of pulmonary invasion, and involvement of the cervical glands. Death occurred from pulmonary hemorrhage. The condition of the tongue was markedly improved after three months’ treatment.

SKIN TUBERCULOSIS, INCLUDING LUPUS. Nourney<sup>109</sup> (1905) and Heermann<sup>110</sup> (1905) reported at the Verein der Aerzte, of Duesseldorf (in 1905), the treatment of a few cases of lupus, with



FIG. 8.—Lupus, after six months’ treatment with B. E. and autogenous vaccine.

satisfactory results. Denys<sup>12</sup> states that all lupus cases are benefited, and a few are completely cured with B. F., and emphasizes the necessity for considering carefully the specific treatment of the secondary streptococcus infections. Wright,<sup>58</sup> Raw,<sup>37</sup> Tod and Western,<sup>131</sup> and Rosenbach,<sup>132</sup> report good results.

The Finnish, Dutch, and Danish reports are not in accord, and are mainly against those of the other observers.

Our cases total 3 “open” and for these the results may be expressed as poor (see Figs. 8, 9 and 10). The 2 cases photographed were also treated with *Micrococcus aureus* and streptococcus vaccines (autogenous).

ORTHOPEDIC. Bone and Joints. Denys<sup>12</sup> records 6 cases of bone tuberculosis treated by Sluyts and von der Bergh, with or

without minor operations as seemed necessary, who considered the cases rapidly cured.



FIG. 9.—Lupus. At beginning of treatment.



FIG. 10.—After six months' treatment.



The secondary streptococcus invasion was found an extremely important factor and, as is well known, retarded healing.

Ridlon<sup>133</sup> (1908) reported on chronic joint cases and Nutt and Hastings<sup>134</sup> after experience with 24 cases of bone and joint infections concluded that tuberculin is of decided value in the treatment of tuberculous joints and bones. It seems the best tonic we have for such patients and has also an effect on the local infection, which cannot be wholly accounted for by improvement in general health. This conclusion remains unchanged after careful study of 65 cases. These cases were "open," with sinuses.

PERITONITIS, TUBERCULOUS. Denys<sup>12</sup> reported 8 cases in 1902, and 8 additional in 1905. Of the 16 cases, 13 were classed as cured, and of the 3 deaths 1 was from acute pneumonitis. Birnbaum<sup>115</sup> reported (1907) 11 cases; 5 with, and 6 without ascites, and Nathan Raw<sup>116</sup> (1910) reported 19 cures out of 26 cases.

Summary of our cases: Five "closed" cases; results good in 3, death in 2.

The report of the following case is of interest on account of the complications, the continuance of tuberculin inoculations during the febrile period (see Fig. 3), and the single course of tuberculin.

CASE IV.—Nanette T., aged seven years. Tuberculous peritonitis, bilateral pleuritis, bronchopneumonia. Peritonitis noted in November, 1909. Operation in December, 1909; failing since operation; hygienic treatment in the city; irregularly intermittent temperature with wide variations to 104° F., pulse 120 to 140 (see Fig. 3). Respiration, 30 to 40. Tuberculin inoculations begun February 1, 1910, and continued until July 10, 1910 (27 inoculations, from 0.1 c.c. of 0.0000001 to 0.6 c.c. of 0.00001); hygienic conditions good; in New York until May, then in the country; apparently cured in August; health excellent in December, 1910; no recurrence or recrudescence in October, 1911.

December, 1909. Operation.

January 31, 1910. Has been failing since operation. Temperature irregularly intermittent, with wide variations to 104° F.; pulse from 120 to 140; respirations from 30 to 40 a minute.

February 1. First tuberculin inoculation, 0.1 c.c. of 0.0000001; inoculations to be given at intervals of four or five days.

February 12. Right pleuritis, with effusion; heart 5 inches to left of midsternal line.

February 17. Dulness lessened over right back; heart 3½ inches to the left of midsternal line.

March 20. During last ten days bronchopneumonia and pleurisy signs over left axilla and left back below spine of scapula.

April 1. Improvement marked; temperature, 100° to 101° F. in afternoon.

April 4. Inoculation of 0.1 c.c. of 0.000001, and following it a general reaction with temperature to 103° F. Inoculations

continued regardless of temperature, since no signs of local reaction over abdomen were evident.

May 20. General health and local condition excellent. Patient moved to the country.

July 10. Last tuberculin inoculation given (0.6 c.c. of 0.00001).

December 1. Health excellent, remains well. Weight, increased from  $48\frac{1}{2}$  pounds to  $62\frac{1}{2}$  pounds, partially accounted for by growth.

INTESTINAL. Seven cases were recorded by Denys<sup>12</sup> in 1905. Of these 3 were febrile, and 1 recovered and 2 died. Of the 4 afebrile cases there are 4 cures. We record 2 "open" cases, with 1 death; 1 intestinal, sigmoiditis death; 1 intestinal, upper colon (?), mesenteric glands involved.

In addition, the 4 following cases were treated with marked improvement in general health and ultimately apparent cure; 3 fistula in ano, 1 perineal tissues and rectum.

ADRENAL TUBERCULOSIS (ADDISON'S DISEASE). Treated 5 "closed" cases. No improvement has been noted under tuberculin therapy. The 5 cases died.

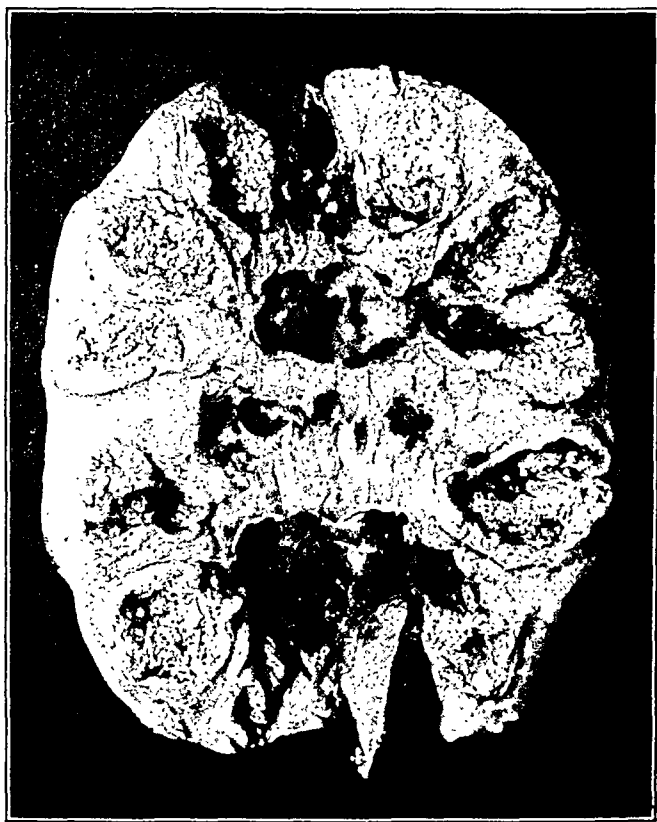


FIG. 11.—After tuberculin inoculations. (Ekehorn, Type i.)

GENITO-URINARY. In 1907, Birnbaum<sup>115</sup> reported excellent results in 4 cases of cystitis, 1 with renal involvement.

Denys<sup>12</sup> (1905) alluded to the excellent results to be expected, and records 1 case of cystitis in a young woman cured after injections from March, 1902, to July, 1905.

Wildbolz,<sup>135</sup> Fullerton,<sup>136</sup> Pottenger,<sup>137</sup> Nathan Raw,<sup>116</sup> Young,<sup>138</sup> Gardner,<sup>139</sup> Walker,<sup>140</sup> report cases, and the general conclusion seems to be that benefit accrues from the increase of the general toxin tolerance. Wildbolz could find in 5 tuberculous kidneys little evidence of scarring.

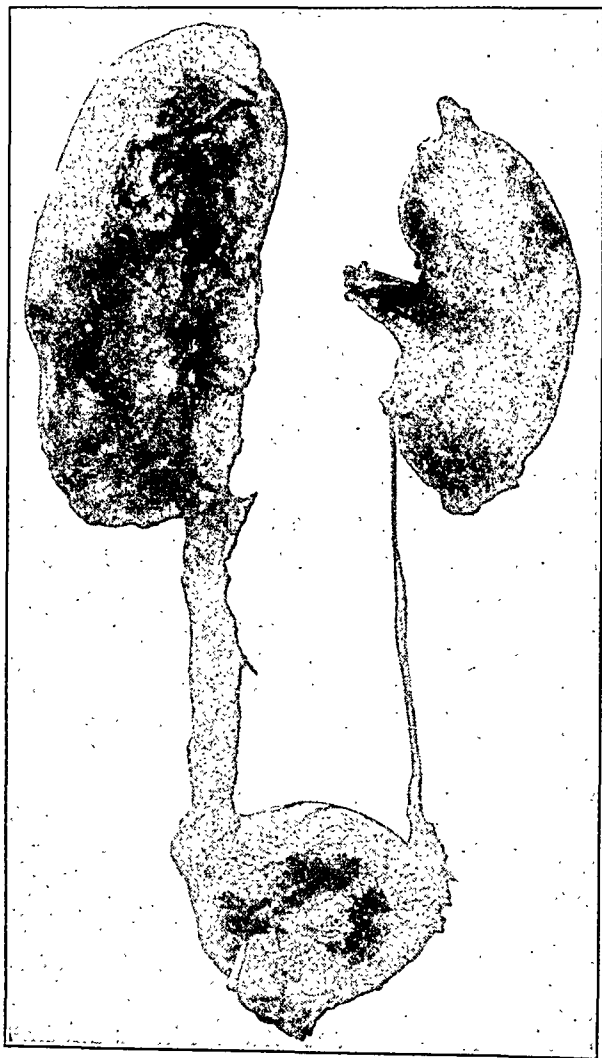


FIG. 12.—Kidney not opened. No tuberculin. No operation. Under observation two years, before death.

Ekehorn<sup>141</sup> recently published an interesting article bearing on the general pathology of renal tuberculosis. It is quoted in detail, for the photographs (Figs. 11, 12 and 13) of 2 of our specimens show his types of lesion. He studied in 33 cases the spontaneous course of the disease, without treatment; 25 died. Of the eight

still living, in whom diagnosis was made eight years ago, on an average, 4 were subjectively healthy, and at times passed a clear urine; but healing was only apparent. In 4 others he states "the process is now rapid and the course will probably be short."

In histological specimens, from section, or late operation, there are two general types of lesion: (1) Kidney changed to cavernous pockets, corresponding to calices, filled with sterile detritus, and parenchyma about all lost (late). (2) The second group is one with a sclerosing process, which involves kidney and surrounding



FIG. 13.—Kidney opened. (Ekehorn, Type ii.)

tissue. At times only a part, as that of the upper third, is involved. Ekehorn concludes that secondary infection from the renal pelvis always follows rupture of the original focus, while the original tubercle-bacillus infection is from the blood.

Since spontaneous healing is a rare exception, nephrectomy is indicated after diagnosis is established. The use of tuberculin is not considered.

**SUMMARY OF GENITO-URINARY CASES.** With renal involvement: Fifteen "open" cases, with 1 death.

Without renal involvement: Sixteen "open" cases, no deaths. Total of 31 cases, with 1 death. Of 3 untreated cases 2 died, 1 was living in 1910. Thirty-four cases in all were observed over a period of four years with 3 deaths, and a majority of them have improved to such a degree that it is safe to say that at the end of eight years, a period corresponding to that of Ekehorn's observations, a much larger percentage will have survived than noted by Ekehorn for cases running a spontaneous course without treatment. Of the 31 cases treated with tuberculin 22 were considered inoperable, 4 were operated upon after the general health was much improved under tuberculin, and 5 were treated with tuberculin after operation.

In 1 case, a patient, aged sixty years, renal tuberculosis in the left kidney was apparently cured by one series of inoculations over a period of seven months, without operation. The infection in the left kidney was proved by ureteral catheterization.

The abstracts of 3 case histories are appended.

CASE V.—Dr. R. W., aged 42 years. Tuberculosis of right kidney, bladder, prostate, and seminal vesicles. Duration 2 years; inoperable. No hygienic treatment, irregular evening temperature. Tuberculin injections from July 30, 1907, to May 9, 1908 (60 inoculations); improvement. Death two months after withdrawing inoculations.

Tuberculin given in two series: First series, dosage up to 0.5 c.c. of 0.0001; second series, dosage up to 1 c.c. of 0.00002.

CASE VI.—Dr. I. D. K., aged twenty-eight years. Tuberculosis of the kidney and bladder, duration two years.

Tuberculin inoculations from May 21, 1908, to September 22, 1909, and from October 2, 1909, to February 3, 1910 (80 inoculations).

February 19, 1910. Pyelitis. Secondary infection. Nephrectomy.

December, 1911. Occasional attacks of frequency of urination. Urine normal and free from tubercle bacilli.

Tuberculosis of the left kidney and bladder was diagnosticated six months before patient was admitted for tuberculin inoculations. The general health was excellent, and the only symptom complained of was frequent micturition for which the patient consulted a specialist, who through cystoscopic examination discovered the tuberculous condition of the kidney and bladder. The urine contained a relatively small number of pus cells and red blood cells, and a large number of tubercle bacilli. Nephrectomy was advised but the patient refused to have operation, and went to Saranac Lake where he remained for six months, during which time inoculations of tuberculin were administered.

May 21, 1908. The first inoculation of first series was given, dosage 0.1 c.c. of 0.000001 B. E.

May 25. Tubercle bacilli demonstrated in the urine.

August 8. Within twenty-four hours after tuberculin inoculation frequency of urine was increased.

August 29. Following tuberculin inoculation on August 22, temperature rose to 101° F., and a general reaction occurred, which lasted two days; one tuberculin inoculation was omitted. Frequency of urination was increased for twelve hours following the inoculation, then suddenly ceased; since August 25; patient states that he never felt better.

September 1. Reported that he was not feeling so well, on account of slight headache and night sweats during the two preceding nights.

September 12. Frequency of urination marked, so that dosage of tuberculin was not increased.

October 3. Frequency of urination diminished, probably in consequence of a few doses of tincture of hyoscyamus.

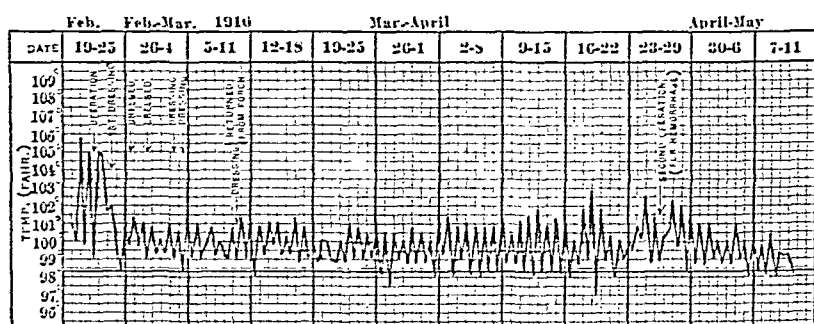


FIG. 14.—Secondary renal infection in renal tuberculosis. Operation.

October 26. After the last 3 inoculations there has been a distinct local reaction, as indicated by the increased frequency of urination; slight hematuria; and pain in the bladder lasting twenty-four hours.

December 11. Frequency of urination much less; feels much better in every way.

December 21. Increased frequency and discomfort again noted after the last dose.

June 28, 1909. Following the inoculation of 0.8 c.c. of 0.0001 on June 18 the temperature rose to 102° F. and lasted for four hours, since when the patient is much improved; the dose reduced to 0.5 c.c. of 0.0001. Since reaching 0.5 c.c. of 0.00001 the inoculations have been given at ten-day intervals.

July 19. Following the inoculation of July 9, 0.5 c.c. of 0.0001 the temperature again arose for a few hours; the dose was reduced to 0.3 c.c. of 0.0001.

Showed a marked increase in weight and improvement in

general condition until the sudden rise of temperature and septic symptoms, which occurred in February, 1910.

February 19, 1910. Patient's temperature suddenly rose from 101° to 105.5° F., and the symptoms and signs of acute septic condition rapidly developed. An operation was immediately performed; the left kidney was removed, and two days following the operation the temperature had again fallen to its former course, that of a remittent temperature from 99° to 101° F.

April 23. Two months after operation, without warning, a severe hemorrhage from the wound occurred, and a second operation was performed, following which the patient was in a precarious condition for ten days.

May 11. Marked improvement was noted; the temperature varies from 98° to 99.5° F., and shortly became normal.

July. Went to Saranac Lake; was given few doses of tuberculin; remained there until early in September.

December 4, 1911. Patient reported in excellent health, excepting an occasional attack of frequent micturition lasting a few hours. Urine normal, tubercle bacilli not found.

CASE VII.—Mr. W., aged 47 years. Tuberculosis of both (?) kidneys, prostate, bladder, and cervical glands; eighteen months (?) duration; inoperable; irregular evening temperature; hygienic surroundings favorable. Tuberculin inoculations from March 9, 1908, to September 17, 1909; dosage 0.2 c.c. of 0.0005; second series, October 7, 1909, to November 2, 1910, dosage to 0.6 c.c. of 0.0001; third series, December 9, 1910, to November, 1911. The general condition is good, gain of 42 pounds in weight is maintained; no tubercle bacilli in the urine.

Was referred by the late Dr. Alexander, in March, 1908. Examination by Dr. Alexander revealed the involvement of both ureteral orifices, the trigonum and extending into the fundus; the process was more extensive on the right side. It was considered that both kidneys were involved, although tenderness with some enlargement was noted only on the right side. The patient had been under treatment for chronic cystitis for over two years, the condition had not improved. There had been a loss of weight of 32 pounds and the patient suffered mostly from severe pain in the pelvis which was referred to the bladder and to the rectum; frequent micturition disturbed rest and sleep, while the pain was controlled by codeine and morphine. Urination occurred at least every hour during the late afternoon, after slight exercise as often as every twenty minutes. The urine was thick with pus and blood and showed a large number of tubercle bacilli. The cervical glands on one side of the neck were enlarged and quite firm, forming a mass extending from the tip of the mastoid to the clavicle on the right side. The local treatment, irrigations with silver nitrate and other drugs, was continued.

Proper hygienic measures were advised—living and sleeping in the open air, suralimentation and rest.

Operation was absolutely contraindicated. Tuberculin inoculations were begun March 9, 1908, with 0.1 c.c. of 0.000001.

July 23, 1908. The general health was much improved; patient complains of severe pain at the neck of the bladder and frequent micturation; on cystoscopic examination no local retrogression noted.

September 9. Bladder irrigations with 1 per cent. silver nitrate have been continued, and following this irrigation there has been severe pain and suppression of urine; dosage of tuberculin more rapidly increased.

December 28. During the last ten days patient suffered from attack of acute rheumatic arthritis; was given large doses of aspirin, which increased the irritation of the bladder; tuberculin inoculations 0.3 c.c. of 0.0001.

March 23, 1909. Cystoscopic examination, pus coming from right ureter, left ureteral orifice normal; the bladder about the trigonum appears normal, prostate only slightly involved.

March 26. On account of persistence of pain and frequent micturition, cultures were taken from the urine which still contained large numbers of tubercle bacilli, and streptococcus was obtained in pure culture. A vaccine was prepared and was inoculated with the tuberculin; following this there was a marked focal reaction in the prostate, with pain, swelling and tenderness which persisted for five days.

April 21. Again an inoculation of streptococcus vaccine was given, 41,000,000; no reaction.

April 27. An inoculation of streptococcus vaccine, 30,000,000 and 0.5 c.c. of 0.0001 of tuberculin was given.

May 18. Forty-eight hours after last dose (May 11) there was a slight focal reaction in the prostate and bladder, so that the dose of streptococcus vaccine was decreased to 27,000,000; the tuberculin was not increased.

June 2. The streptococcus vaccine discontinued; marked improvement in the sensitiveness of the trigonum and in the frequency of micturition, which followed the first three doses of streptococcus vaccine.

June 21. Since withdrawal of the streptococcus vaccine (June 2) pain in the bladder, burning micturition and the frequency have increased markedly. Fresh streptococcus vaccine was prepared, which was not used until August 9, for it was considered that the symptoms depended solely on the tuberculous process.

September 17. The vaccine and tuberculin have been continued since August 9. Tuberculin and vaccine now discontinued for three weeks; the symptoms seemed intensified so definitely following



the injection of tuberculin that it was decided to return to small doses after three weeks.

October 7. Tuberculin inoculations resumed, with a dose of 0.1 c.c. of 0.000005.

October 16. Since September 17 (during the time he was receiving no tuberculin or vaccine) symptoms were aggravated and rest and sleep were disturbed on account of frequent micturition which occurred as often as fifty (?) times in one night.

November 9. The dosage of tuberculin has been very slowly increased, resulting in less improvement in his symptoms; for short periods of from two to three hours during the day the urine was voided every ten minutes, and such an attack was followed by intense burning pain in the bladder, which lasted throughout the rest of the day. Intense pain in the bladder occurs also after defecation; a few small clots of blood have been passed in the stools; examination revealed the presence of hemorrhoids; the urine no longer contains blood macroscopically, but is filled with mucus and pus; there has been no fever for the last few weeks, but the sweating continues.

December 7. Dr. Alexander refused to make a cystoscopic examination, on the ground that his general condition was excellent, and that both kidneys were originally involved, and since the bladder symptoms were better he would not make a cystoscopic examination. Since his symptoms had not ameliorated during the last eight weeks, on December 1, the dosage of tuberculin was reduced to 0.1 c.c. of 0.000001.

May 16, 1910. General condition excellent; weight, 142 pounds, a gain of 32 pounds; feels well, but still complains of, for him, a moderate frequency of micturition. Reported to Dr. Alexander who advised him to persist with the tuberculin therapy.

October 25. Dosage of tuberculin inoculation 0.5 c.c. of 0.0001; during the last week, has complained of frequent micturition, for the first time in months. The urine is cloudy, contains a few small granular masses consisting of leukocytes; tubercle bacilli could not be demonstrated; the method of demonstrating the tubercle bacilli was the same as for the previous examinations made since March, 1908. A careful search was made of the stained specimen of pus after centrifugation, and the pus was also inoculated into guinea-pigs; later on, the antiformin method was employed.

November 2. Dosage of tuberculin 0.6 c.c. of 0.0001; has complained again, during last week, of frequent micturition and of burning on micturition, and also of a dull heavy ache which radiates down to the pubes. The tuberculin discontinued for six weeks, at the end of which time a third series of 0.2 c.c. of 0.000001 was advised.

November 30. Symptoms have improved; short attacks of painful urination occur but seldom; his weight is above his former

usual weight of 130 pounds; for some months he has been able to attend to work which calls for little exertion.

December 9. Third series of tuberculin inoculations begun with 0.2 c.c. of 0.000001.

January 19, 1911. Since last visit has gained 7 pounds in weight; feels much stronger than he has felt in years; no dysuria and no frequent micturition; the urine is practically clear and contains no tubercle bacilli. The patient has been returning very irregularly for tuberculin inoculations because he feels so well, and has received no tuberculin inoculation since December 9, six weeks ago.

March 1. Still gaining in weight; feels stronger; during the last few weeks dysuria has not returned.

May 9. Dosage of tuberculin inoculation 0.5 c.c. of 0.000001; weight, 143 pounds; frequency of micturition slightly increased during the last few weeks.

July 26. The patient has returned for tuberculin inoculations at intervals of six or seven weeks; inoculation of 0.5 c.c. of 0.000001, and was advised to discontinue the inoculation unless he could return more frequently.

October 23. Complains that he has not felt so well for a week, although the local symptoms of his tuberculous disease have abated. The urine is free from tubercle bacilli and shows only a few leukocytes; tuberculin inoculations have been discontinued.

December 2. Tuberculin injections begun again, 0.1 c.c. of 0.000001. General health excellent; frequent micturition occasionally occurs and lasts for a few hours; urine free from tubercle bacilli.

TUBES AND PELVIC ORGANS (GYNECOLOGICAL). Such cases have been reported upon favorably by Birnbaum<sup>115</sup> (1907), and by Nathan Raw<sup>116</sup> (in 1910). We have had no experience with such cases.

MILIARY TUBERCULOSIS. One may quote Denys:<sup>12</sup> "The process is too rapid to be influenced by B. F.," and one may add by any other kind of tuberculin. The specific therapy for miliary disease will, if it comes, not be a process of active immunization but one of passive immunization, with some particular serum or chemotherapy.

#### CONCLUSION.

SECONDARY INFECTION MODIFIES. From the nature of the process of active immunization one should expect the results with tuberculin in surgical tuberculosis to be much the same with all anatomical types, and such is the fact. The one modifying factor, aside from that of the individual's response is that of secondary infection, and one may state that "closed" cases, in the sense of Petruschky, do well; and often cases vary according to the summa-

tion of toxic effects from the tubercle bacillus and the secondary invaders.

In surgical conditions the secondary invader is not so to be feared as in the pulmonary and pleural conditions, and the secondary invasions in surgical conditions always call for some other than tuberculin treatment. We may again recall the patience and perseverance exemplified by Petruschky in dealing with such cases and conclude with him that in Koch's tuberculin we have a valuable agent for treating incipient tuberculosis; and may add that until specific therapy has been tried one should never despair of a seemingly hopeless case.

# BIBLIOGRAPHY.

1. Koch. Deutsch. med. Woch., 1890, No. 46, pp. 1029 to 1032; *ibid.*, 1891, No. 3, p. 101.
2. Trudeau. Med. Rec., 1890, xxxviii, 565; Med. News, 1892, lxi, 253, 255, 258; *ibid.*, 298; Internat. Med. Mag., 1892, i, 1129.
3. de Schweinitz. Med. News, 1894, lxxv, 625; Trans. Assoc. Amer. Phys., 1897, xii, 205; de Schweinitz and Schroeder, United States Dept. Agricult., Bureau Animal Industry, 1896, Bull., No. 13; de Schweinitz and Dorset, New York Med. Jour., 1897, lxxv, 105; de Schweinitz, Dorset, and Schroeder, Amer. Med., 1902, iv, 850.
4. Petruschky. Deutsch. med. Woch., 1891, No. 13, p. 485; Vorträge z. Tuberkulose Bekämpfung, 1897, No. 1; Deutsch. med. Woch., 1897, No. 39, p. 620; No. 40, p. 639; Koch's Tuberkulin und seine Anwendung beim Menschen, Berlin, 1904, pp. 1 to 35, reprint from Berlin. Klinik, 1904, Heft 188.
5. Goetsch. Deutsch. med. Woch., 1901, No. 25, p. 405; *ibid.*, 1909, No. 26, p. 1170.
6. Müller. Wien. med. Woch., 1905, lv, 2297, 2349.
7. Turban. Bericht über die II Versammlung der Tuberkulose-Aerzte, Berlin, 1904, xi; Beiträge z. Kenntnis der Lungen Tuberkulose, Wiesbaden; The Diagnosis of Tuberculosis of the Lung, with Special Reference to the Early Stages. New York, 1906.
8. Weicker. Wien. med. Woch., 1907, lvii, 2318, 2367, 2427, 2468.
9. Spengler. Deutsch. med. Woch., 1904, No. 31, p. 1129; *ibid.*, 1905, No. 31, pp. 1228, 1353; Zentralbl. f. Bakt., 1907, xlv, 481 to 485.
10. Baudäch. Deutsch. med. Woch., 1897, No. 34, p. 544.
11. Trudeau. AMER. JOUR. MED. SCI., 1907, cxxxiii, 813.
12. Denys. (Louvain, ed.) 1905, pp. 66, 218, 236, 264, 271, 278, 292, 300, 301, 306, 313, 314, 316.
13. Sahli. Cor.-Bl. f. Schweiz. Aerzte, 1906, Nos. 12 and 13, pp. 373, 417, reprint. p. 16.
14. Hammer. Brauer's Beitr. z. Klin. d. Tuberk., vii, 179; Deutsch. med. Woch., 1907, No. 34, p. 1387; Wien. med. Woch., 1903, liii, 2343.
15. Hamman and Wolman. Johns Hopkins Hosp. Bull., 1909, xx, 225.
16. Hyslop-Thomson. British Med. Jour., 1909, i, 136.
17. Lowenstein. Deutsch. med. Woch., 1910, No. 36, p. 1654.
18. Turton. Practitioner, 1907, lxxix, 650; AMER. JOUR. MED. SCI., 1908, cxxxv, 610.
19. Bonney. Trans. Nat. Assoc. for the Study and Prevention of Tuberculosis, June, 1908, p. 159.
20. Pottenger. The Diagnosis and Treatment of Pulmonary Tuberculosis with Tuberculin, 1908.
21. Bandelier and Roepke. Specific Diagnosis and Therapy, 1909; Beitr. z. klin. d. Tuberkulose, 1910, xv, 1 to 175; AMER. JOUR. MED. SCI., 1910, cxl, 140.
22. Raw. Lancet, 1911, i, 927.
23. Dluski. Beitr. z. klin. d. Tuberkulose, 1908, x, 41 to 125.
24. Kohler. Internat. Tuberculosis Cong. at Paris, 1905.
25. Birnbaum. Das Kochische Tuberkulin in der Gynäkologie und Geburtshilfe, Berlin, 1907, pp. 1 to 125.
26. Beitzke. Virchow's Archiv, 1907, Beiheft zum exc, 58.
27. Daels. Virchow's Archiv, 1907, Beiheft zum exc, 90.
28. Klebs. Virchow's Archiv, 1907, Beiheft zum exc, 134, 541.
29. Koch, Max. Virchow's Archiv, 1907, Beiheft zum exc, 246.
30. Orth and Rabinowitsch. Virchow's Archiv, Beiheft zum exc, 1.

31. Luedke. Wurtzberger Gesamtgebiet der practischen Medicine, 1907, vii, 223.
32. Kohler and Lenzmann. Beihefte z. med. Klinik, 1909, Pt. 2, p. 29.
33. Liebmann. Virchow's Archiv, 1896, Supplementheft zum cxliv, 123 to 203.
34. Latham. Lancet, 1910, ii, 887.
35. Emery. Immunity and Specific Therapy, London, 1909, pp. 284, 314 376, 354.
36. Walters. Lancet, 1910, ii, 887.
37. Raw. Brit. Med. Jour., 1910, i, 1539.
38. Calmette and Breton. Compt. rend. Acad. des Sci., 1909, cxlii, 616; Calmette and Guérin, La Presse Médicale, 1906, p. 380; Calmette, Specificsches Diagnostik und Therapie der Tuberkulose, 1909, p. 169.
39. Beraneck. Compt. rend., Hebdom., 1903, cxxxvii, 889.
40. Rosenbach. Deutsch. med. Woch., 1910, No. 33, p. 1513; *ibid.*, No. 34, p. 1553.
41. Spengler. Deutsch. med. Woch., 1908, No. 38, p. 1620; *ibid.*, 1909, No. 49, p. 2172.
42. Maragliano. Berl. klin. Woch. 1906, No. 43, p. 1391.
43. Wassermann and Brueck. Deutsch. med. Woch., 1906, No. 12, p. 449.
44. von Behring. Rec. de méd. int., Paris, 1902, ix, 759; Lancet, 1905, ii, 1126 (editorial, p. 1115); The Suppression of Tuberculosis, etc., New York, 1904.
45. Webb. Jour. Med. Research, 1909, xx, 1 to 25.
46. Bordet and Gengou. Compt. rend Acad. des Sc., 1903, cxxxvii, 351; Gengou, Compt. rend. Soc. de biol., 1906, lviii, 218; Berl. klin. Woch., 1906, No. 48, p. 1531.
47. Dembinski. Compt. rend. Soc. de biol., 1904, ii, 502.
48. Trudeau. AMER. JOUR. MED. SCI., 1907, cxxxiii, 813.
49. Bordet and Gengou. Annals de l'Institut Pasteur, 1901, xv, 290.
50. Lowenstein und Rappoport. Zeitschr. f. Tuberk. u. Heilstattenn, 1904, v, 485 to 535; Lowenstein und Rappoport. Babes, Ehrlich, quoted from Wassermann und Brueck, Deutsch. med. Woch., 1906, No. 12, p. 449; Lowenstein und Rappoport, Beitr. z. Klinik. d. Tuberk., 1905, iii, 417.
51. Marmorek. La Presse Med., 1909, ii, 12.
52. Sahli. Cor.-Bl. f. Schweiz. Aerzte, 1906, No. 12, p. 373; *ibid.*, No. 13, p. 417.
53. Maragliano. Wassermann and Brueck quoted by Sahli, Cor.-Bl. f. Schweiz. Aerzte, 1906, No. 12, p. 373; No. 13, p. 417.
54. Metchnikoff, Baumgarten, Sanarelli, Kanthac, Hardy, and Wright, quoted by Emery. Immunity and Specific Therapy, London, 1909, pp. 239 to 300.
55. Denys and Leclef. La Cellule, 1895, ii, 177, quoted by Emery.
56. Mennes. Zeitsch. f. Hyg., 1897, xxv, 413; Markl, Zeitsch. f. Hyg., 1903, xlii, 244; Zentralbl. f. Bakt., 1905, xxxviii, 69.
57. Neufeld and Rimpau. Deutsch. med. Woch., 1904, No. 40, p. 1458.
58. Wright. Lancet, 1910, ii, 863, 885.
59. Mueller. Vorlesungen über Infektion und Immunität, Jena, 1909, p. 134.
60. Wright and Douglas. Proc. Royal Soc. London, 1904, lxxii, 357; *ibid.*, 1905, lxxiv, 159; Bullock and Atkin, *ibid.*, lxxiv, 379.
61. Torrey. Jour. Med. Research, xxii, 95.
62. Hektoen. Jour. Infect. Dis., 1906, iii, 434; Rosenow, Jour. Infec. Dis., 1907, iv, 285.
63. Von Pirquet. Wien. klin. Woch., 1903, No. 26, p. 758; No. 45, p. 1244.
64. Wolff-Eisner. Die Ophthalmologie und Kutan Diagnosis, Würzburg, 1908, p. 112.
65. Citron. Berl. klin. Woch., 1909, No. 51, p. 2288.
66. Trudeau, Baldwin, and Krause. Jour. Med. Research, 1910, xxii, 189 to 273; Krause, *ibid.*, 1911, xxiv, 361.
67. Koch. Tenth Internat. medicin. Kongress, Berlin, 1890; Deutsch. med. Woch., 1890, No. 46a, p. 1029; *ibid.*, 1891, No. 3, p. 101; *ibid.*, No. 17, pp. 1189 to 1192.
68. Hunter. British Med. Jour., 1891, ii, 169.
69. Trudeau. Med. News, 1892, lxi, 256.
70. Koch. Deutsch. med. Woch., 1897, No. 14, p. 209.
71. Koch. Deutsch. med. Woch., 1901, No. 48, p. 829.
72. Dluski. Przegląd lekarski, 1910, xlv, 23; Deutsch. med. Woch., 1910, No. 35, p. 1626.
73. Denys. LeBouillon Filtre, 1905, pp. 13 to 14.
74. Landmann. Zentralbl. f. Bakt., 1900, xxvii, 870; Buchner and Hahn, Münch. med. Woch., 1897, xlviii, 1343.
75. Von Behring. Loc cit., ref. 44. (Lancet.)
76. Hirschfelder. Trans. Med. Soc. California, 1897, xxvii, 251; Deutsch. med. Woch., 1897, Ther. Beilage, No. 4, p. 25.
77. Klebs. Wien. med. Woch., 1891, No. 15, p. 641; Zentralbl. f. Bakt., 1896, xx, 488; Zeitsch. f. kausal Therap., Bremerhaven, 1905, ii, 14 to 24; Deutsch. Med. Woch., 1907, No. 15, p. 577; *ibid.*, 1908, No. 3, pp. 97 to 100.

78. Piorkowski. *Tuberculo albumin*, 1908.
79. Deycke und Reschad Bey. *Deutsch. med. Woch.*, 1905, No. 12, p. 489; No. 14, p. 545. *ibid.*, 1907, No. 3, p. 89.
80. Von Ruck. *Med. Rec.*, 1906, lxi, 85; *ibid.*, 1907, lxxii, 383; *Zeitschr. f. Tuberk.*, 1906, viii, 377; *ibid.*, 1907, xi, 493.
81. Siegesmund. *Ztschr. f. Hyg. und infek. Krank.*, 1910, lxvi, 357; *Deutsch. med. Woch.*, 1910, No. 43, p. 2020.
82. Spengler. *Deutsch. med. Woch.*, 1904, No. 31, p. 1129; *ibid.*, 1905, No. 31, pp. 1228, 1353; *ibid.*, 1907, No. 9, p. 337.
83. Spengler. *Deutsch. med. Woch.*, 1908, No. 38, p. 1620.
84. Landmann. *Berl. klin. Woch.*, 1908, No. 45, p. 2017; *Deutsch. med. Woch.*, 1908, No. 48, p. 2087; Hollos, *Ztsch. f. exper. Path. und Ther.*, 1910-11, viii, 667.
85. Hewlett. *Lancet*, 1910, ii, 886.
86. Citron. *Berl. klin. Woch.*, 1909, No. 51, p. 2289.
87. Garbat and Meyer. *Zeitsch. f. exper. Path. und. Ther.*, 1910, viii, 1.
88. Gordon. *Deutsch. med. Woch.*, 1910, No. 38, p. 1746; *ibid.*, 1911, No. 3, p. 125.
89. Jochmann and Möllers. *Deutsch. med. Woch.*, 1910, No. 46, p. 2141; *ibid.*, 1911, No. 3, p. 127.
90. Gabrilowitsch. *Deutsch. med. Woch.*, 1911, No. 3, p. 126.
91. Wolff-Eisner. *Berl. klin. Woch.*, 1910, No. 47, p. 2147.
92. Meyer. *Berl. klin. Woch.*, 1911, No. 2, p. 69.
93. Calmette and Guerin. *Ann. de l'Institut. Pasteur*, 1907, xxi, 525 to 532; *Echo. méd. du nord.*, Lille, 1906, x, 257; Calmette and Breton, *La Presse Médicale*, 1906, p. 183; *Compt. rend. Acad. des Sci.*, 1906, cxlii, 616; *La Presse Médicale*, xvi, 833.
94. Moeller. *Münch. med. Woch.*, 1908, No. 45, p. 2324; *Deutsch. med. Woch.*, 1908, No. 48, 2089.
95. Hyslop Thomson. *British Med. Jour.*, 1909, i, 136.
96. Walters. *Lancet*, 1910, ii, 887.
97. Lissauer. *Deutsch. med. Woch.*, 1907, No. 33, p. 1335.
98. Inman. *Lancet*, 1910, ii, 889.
99. Lawson. *Lancet*, 1910, ii, 889.
100. Brown. *Kleb's Tuberculosis*, 1909, p. 540.
101. Trudeau. *Jour. Amer. Med. Assoc.*, 1909, lii, 261.
102. Wright. *Lancet*, 1910, ii, 869.
103. Leishmann. *Lancet*, 1910, ii, 888.
104. Reyn and Kyer-Peterson. *Lancet*, 1908, i, 919, 1000.
105. Hastings. *Trans. Sixth Internat. Cong. on Tuberculosis*, 1908, i, pt. i, 387.
106. Von der Weij. *Ref. from Deutsch. med. Woch.*, 1910, No. 42, p. 1970.
107. Von Hippel. *Deutsch. med. Woch.*, 1904, No. 28, p. 1041.
108. Dorschlag. *Monograph, Casuistischer Beitrag z. Tuberkulinbehandlung der Tritis tuberkulosa*, Greifswald, 1905.
109. Nourney. *Deutsch. med. Zeit.*, 1905, xxvi, 201.
110. Heermann. *Zeit. f. Krankenpflg.*, 1904, xxvi, 177, 229, 257, 273.
111. Bulloch. *Lancet*, 1905, ii, 1604.
112. Kraemer. *Monograph, Das Prinzip der Dauerheilung der Tuberkulose*, Tübingen, 1904.
113. Walker. *British Med. Jour.*, 1908, ii, 559.
114. Kohler and Lenzmann. *Beihefte z. med. Klinik*, 1909, Pt. 2, p. 55.
115. Birnbaum. *Zentralbl. f. Gynäk.*, 1907, xxxi, 1174; *Monograph, Das Kochschen Tuberkulin in der Gynäkologie und Geburtshilfe*, Berlin, 1907.
116. Raw. *Lancet*, 1910, i, 844 to 848.
117. Hartwell and Streeter. *Boston Med. and Surg. Jour.*, clxii, 409.
118. Thomas. *Jour. Amer. Med. Assoc.*, 1910, liv, 371.
119. Winslow. *Laryngoscope*, Nov., 1909, reference from *Jour. Amer. Med. Assoc.*, liv, 80.
120. Peter. *Med. Rec.*, 1910, lxxvii, 14.
121. Clark. *Jour. Cutan. Dis.*, 1909, xxvii, 567.
122. Pottenger. *AMER. JOUR. MED. SCI.*, 1906, cxxxii, 906.
123. Jurasz. *Deutsch. med. Woch.*, 1907, No. 27, p. 1073.
124. Snell. *British Med. Jour.*, 1907, i, 317.
125. Bruechner. *Arch. f. Augenheil*, reference from *Deutsch. med. Woch.*, 1908, No. 14, p. 566.
126. Bull. *Jour. Amer. Med. Assoc.*, 1907, xlix, 377.
127. Darier. *Rev. de Therap.*, 1903, lxx, 37.
128. Dor. *Klin. therap. Woch.*, 1910, xvii, 570.
129. Derby. *Trans. Cong. Amer. Phys. and Surg.*, 1910, viii, 82.

## 426 HASTINGS: TUBERCULIN THERAPY IN SURGICAL TUBERCULOSIS

130. Herrenschwand. *Archiv f. Augenheil.*, 1911, lxxviii, 33.
131. Tod and Western. *Practitioner*, 1908, lxxx, 703.
132. Rosenbach. *Deutsch. med. Woch.*, 1910, No. 33, p. 1516.
133. Ridlon. *Jour. Amer. Med. Assoc.*, 1908, l, 75; *Proc. Cong. Amer. Phy. and Surg.*, 1910, viii, 334.
134. Nutt and Hastings. *Amer. Jour. Orthopedic Surg.*, 1908, vi, 48.
135. Wildbolz. *Berl. klin. Woch.*, 1910, No. 26, p. 1215; reference from *Deutsch. med. Woch.*, 1910, No. 27, p. 1291.
136. Fullerton. *British Med. Jour.*, 1910, ii, 71.
137. Pottenger. *California State Med. Jour.*, 1910, viii, 84.
138. Young. *Trans. Cong. Amer. Phy. and Surg.*, 1910, viii, 322.
139. Gardner. *Trans. Cong. Amer. Phy. and Surg.*, 1910, viii, 311.
140. Walker. *Practitioner*, 1908, lxxx, 723.
141. Ekehorn. Reference from *Deutsch. med. Woch.*, 1910, No. 28, p. 1338.

## REVIEWS

---

RECENT METHODS IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS.  
(THE WASSERMANN REACTION AND EHRLICH'S SALVARSAN,  
"606.") By C. H. BROWNING, M.D., Lecturer on Bacteri-  
ology in the University of Glasgow, and IVY MCKENZIE, M.D.,  
Director Western Asylums' Research Institute, Glasgow.  
Pp. 303. Philadelphia and New York: Lea & Febiger, 1912.

THIS book deals exclusively with the Wassermann reaction, salvarsan treatment, and the effect of the treatment on the individual and his serum reaction. It is the most detailed study of the syphilis reaction that has so far appeared in English. The basic principles of hemolysis, specific and non-specific absorption of complement, and the theories of the Wassermann reaction are briefly and clearly analyzed. The preparation of each reagent with the sources of fallacy incident to them and their quantitative differences are studied. Crude antigen extracts are compared as to their antigenic power, with pure lipoids or mixtures of cholesterin, testing them in the presence of the same serums, both syphilitic and normal.

Because of the importance of the reaction in diagnosis, treatment, and prognosis, the emphasis upon the physicochemical factors entering into and influencing the reaction are strongly emphasized. The effort of these workers to introduce a technical modification in the line of greater accuracy deserves much consideration. Their method permits a balanced study of the various antigens and shows: (1) The amount of complement absorption; (2) the delicacy of the various antigen mixtures to weakly reacting syphilitic serums, and (3) the greater uniformity of a lecithin cholesterin mixture as an antigen.

To the clinical application of the tests no undue space is allotted. The importance of the reaction being now generally admitted, the results of most of the workers is briefly reviewed, with the suggestion of some possible clinical problems.

The second half of this work is restricted to the therapeutic agent salvarsan. The history of the brilliant experimental and chemical work which developed rapidly after the recognition by Ehrlich and Berthein of the chemical constitution of atoxyl, is fully given together with a description of the chemical constitution of the

drug salvarsan and of the changes occurring during its preparation for injection. The effect of this drug in the treatment of all forms of syphilis and parasyphilis and those few other conditions in which it has been used are described with many examples and a full review of the literature. The ordinary and accessory after-effects with a conscientious collection of details in the fatal cases so far recorded, have led to the conclusion that, even in those cases in which the drug could be held as the determining factor in the death, the contraindications so often emphasized, were present.

The book is clearly and convincingly written, most of the important theories and studies of the reaction are stated and critically examined. The importance of the reaction both for diagnosis and for the result of treatment is accentuated in every possible way and the need of methods of greater accuracy emphasized. The sincerity of the work is felt throughout and the concise summaries at the end of each chapter are of distinct value. E. P. C. W.

---

HEALTH AND MEDICAL INSPECTION OF SCHOOL CHILDREN. By WALTER S. CORNELL, M.D., Director of Medical Inspection of Public Schools; Philadelphia; Lecturer on Child Hygiene, University Hospital; Director of Division of Medical Research, New Jersey Training School for Feeble Minded. Pp. 614; 200 illustrations. Philadelphia: F. A. Davis Company, 1912.

PREVENTIVE medicine must necessarily deal directly with the young for only by checking up and treating the beginning defects and diseases of children can we hope to develop stronger and more healthy adults. Cornell has made a valuable contribution to the science of preventive medicine in the present volume. Heretofore, parents or family physicians either from lack of knowledge or carelessness overlooked the minor ills of children until the latter were more or less incapacitated by them. Municipal authority is now wisely endeavoring to do this neglected work by means of school inspection, visiting nurses, and by public lectures and exhibits. The results of this systematic supervision of the health of our school children will be far reaching in the improvement of the general health of the community.

The author has been a pioneer in this work and the present volume is based on his six years experience as a medical inspector and the study and examination of over 35,000 children.

In the first division of the work the subject of medical inspection is taken up from various standpoints. This discussion is thorough and complete and contains many useful criticisms of the present methods with suggestions for their correction. In the second division under the heading Hygiene, the subjects of illumination,



ventilation, physical education, and recreation are discussed. In the third division on Defects and Diseases, making up about half of the book, the various divisions of the physical examination are taken up in detail. Practical methods of examination are given with short descriptions of some of the commoner conditions found.

The work is unusually well systematized, the subjects lead up to each other in a logical order and the subject matter deals at all times with practical things. The author wisely emphasizes the fact that after all the success of the work of medical inspection depends on the inspector and his ability to confine himself to essential parts of the work, not to overlook important conditions on the one hand, or to become too much involved in unnecessary details on the other.

The work should be of interest to any physician or student of medicine, but especially to those about to enter inspection work or social service. To such it will serve as a book of instruction, and the valuable criticisms and suggestions point the way along which this important work may be improved and perfected.

F. H. K.

---

TUMORS OF THE JAWS. By CHARLES LOCKE SCUDDER, M.D., Surgeon to the Massachusetts General Hospital; Lecturer on Surgery in the Harvard Medical School, etc. Pp. 391, 353 illustrations. Philadelphia and London: W. B. Saunders Co., 1912.

DR. SCUDDER appears to have been studying the subject of tumors of the jaws for a number of years, and he has collected a vast amount of valuable information. The volume is replete with clinical material (largely original), comprising both the patients' histories and illustrations showing their appearance at various stages of their disease, as well as the results of operation and of the pathological study of the tissues removed.

The work is divided into nine chapters: The first is on epulis; then follow chapters on sarcoma, benign tumors, the odontomas, and carcinoma. Then there is an excellent chapter on diagnosis and operative treatment. Finally, a short chapter on tumors of the palate, and closing chapters on leontiasis ossea, and on prosthesis. The chapter on leontiasis is based largely on the work of Kanavel.

Scudder is less pessimistic than is Bloodgood about the more malignant types of sarcoma of the jaws, and urges extremely radical operation which he does not agree with Bloodgood in regarding as useless either in prolonging life or in affording a hope of ultimate cure.

Less attention is paid to microscopic pathology, as is quite proper in a work of this kind, than to gross pathology, which is well considered. When one studies the book hard, the clinical symptoms on which diagnosis is based become apparent; but a little or rather a good deal of condensation would do the volume no harm. There are so few words on a page, and the pages are so cut up by illustrations and the insertion of case histories (most of them undated, and all in full-sized type), as well as by what seems to us needless elaboration of display typing and enumeration of facts seriatim, that it is difficult to follow the author's thesis. Dr. Scudder is too modest in his exegesis, and his volume is not sufficiently dogmatic to claim for itself the recognition it merits. But as the work is not intended for a text-book, and as the subject is well worthy of serious and painstaking study, these features may well be condoned. There is no doubt that every teacher of surgery, no matter how experienced he may be, as well as every practical surgeon, will be able to glean an immense amount of valuable information from this volume, if he takes sufficient trouble.

A. P. C. A.

---

DISEASES OF THE STOMACH. By MAX EINHORN, M.D., New York Post-graduate Hospital. Fifth edition; pp. 531; 112 illustrations. New York: William Wood & Co.

WHEN a medical book runs into five editions in sixteen years it is *prima facie* evidence that it is good and has been favorably received by the profession.

Einhorn's *Diseases of the Stomach* is written on a comprehensive plan and in rather a (perhaps too) personal vein. The author discusses his subject in successive chapters dealing with anatomy and physiology, methods of examination, diet, local treatment of the stomach; then follows four chapters devoted to organic diseases of the stomach, exhibiting constant lesions, then three chapters covering functional diseases with variable lesions, and individual chapters in which are discussed abnormalities in size, shape, and position of the stomach, nervous affections of the stomach, and the condition of the stomach as seen in diseases of the other organs.

For a book of this character and scope some of these chapters is far too brief and elementary, notably those on diet, anatomy, and physiology, while others are discussed at too great length, giving space to theories and methods that are inaccurate, obsolete, and unscientific.

It is noticeable that the author advocates the use of many special instruments, several of which in the hands of other careful investigators have failed to give accurate and have often given misleading results.

It is to be much regretted that in this last revised edition the literature has not been brought more up to date; few of the references appended being as recent as 1906, while the great majority date back from ten to twenty years ago.

One other criticism: For a book of this character the illustrations are much below standard, and such as there are would be improved and much more intelligently understood had the special points of interest to which the author draws attention been more clearly indicated.

These criticisms should not detract from the acknowledged worth of this book, written by a man who has done so much to blaze the trail through the labyrinth of gastric diseases, and they are offered only in the hope that in the future editions that must follow this one, these faults will be corrected.

V. L.

---

THE DISEASES OF INFANTS AND CHILDREN. By EDMUND CAUTLEY, M.D. Cantab., F.R.C.P. Lond., Senior Physician to the Belgrave Hospital for Children; Physician to the Metropolitan Hospital, etc. Pp. 1042. New York: Paul B. Hoeber.

THE object of the author in writing this book, as stated in the preface, was to "describe the ailments of children in a form suitable for the general practitioner of medicine and sufficiently detailed to render further reference to other works unnecessary, except in the case of unusually rare diseases. . . . The descriptions of some common ailments have been curtailed inasmuch as in a book for graduates it is unnecessary to amplify the minutiae of symptoms." For the same reason, illustrations and charts have been omitted, the author holding that the kindergarten method of teaching, advantageous for the student, may prove a disadvantage to those in active practice for "the expectation of seeing the typical cases of pictorial illustration increases the danger of overlooking those early stages in which disease is amenable to treatment." If that is a valid reason for omitting well-chosen illustrations in a book for graduates, such an argument would apply with even greater force to the instruction of medical students, since they have not the experience to correct a wrong impression conveyed by an illustration. However, between a book padded with illustrations and one devoid of them, the latter is undoubtedly preferable for, after all, the best illustrations for the text are those furnished to the mind's eye of the reader out of his own experience.

The main fault we have to find with this work is the literary style in which most of it is written—abrupt and jerking. This is probably due to the effort at condensation and perhaps arises also from consulting many authorities, for when the author writes

from his own experience as in the valuable chapter on congenital pyloric stenosis the language flows more smoothly. Occasionally the author's meaning is ambiguous; thus, on page 239 he says: "Nearly all infants with adenoids are rachitic, but rachitic children are constantly [frequently (?)] free from adenoids;" and unusual words like "merrythought" would send nine out of ten American physicians to the dictionary. Typographical errors are rather frequent, the most amusing one being "fetal incontinence;" and Latin terms are often not italicized.

But, the above defects have not prevented the author's extensive experience and ripe judgment from making every page valuable, and the whole subject of pediatrics is covered in such a way that the book is excellent as a work of reference for the general practitioner. It is interesting to note that the author prefers cane sugar to milk sugar in infant feeding and opposes the use of "one cow's milk." He explains in a clear way how to dilute mixtures with low proteid percentages may cause indigestion with the appearance of curds in the passages, there being not enough casein to use up the acid of the gastric juice so that the uncombined acid attacks the curd already formed, making it tougher and more resistant to the action of the digestive ferments. The existing confusion in the nomenclature of the milk proteins is regretted and a helpful explanation of the terms is given. The calorimetric method of regulating the diet is described briefly and dismissed with the comment "These calculations are interesting, but not of very much value in practice."

In discussing infant mortality the interesting statements are made that the lowest death rate is found in the British peerage and the fishers of the Faroe Islands, and that "overlaying" kills 1500 infants yearly in England and Wales. This latter statement would make it seem that there is culpable if not criminal negligence, in view of the comparative rarity of such an accident elsewhere.

It is good to see emphasis laid on the value of opium as soon as the diagnosis of intussusception is made; on the need for laxative medicines at times in overcoming constipation in infants; on the importance of giving large doses of antitoxin early in diphtheria; and on the possibility of breathing exercises causing deformities of the chest in rachitic children with adenoids.

The section on the nervous system is commensurate with the importance of the subject, especially from the standpoint of the general practitioner who will find many helpful suggestions in it.

The author is non-committal on the existence of Dukes' fourth disease giving a short description but saying that the evidence is in favor of some epidemics being cases of mild scarlet fever. Like most of us, he has probably never seen anything that suggested the existence of the fourth disease. We cannot agree with the author in the apparent importance which he attaches to doctors,

attendants, and cats in the dissemination of measles, but we are in entire accord with him in his judgment of drug values in the treatment of pertussis.

A. H.

---

THE NEW PHYSIOLOGY IN SURGICAL AND GENERAL PRACTICE.  
By A. RENDLE SHORT, M.D., B.S., B.Sc., F.R.C.S., Registrar  
Bristol Royal Infirmary; Senior Demonstrator of Physiology,  
University of Bristol. Pp. 201. New York: William Wood  
& Co.

THE author has presented a book to the medical world of a character, varied and diverse in the number and variety of subjects dwelt upon. Dealing primarily with physiology, we find nevertheless a smattering of pathology, a bit of histology, a modicum of clinical diagnosis, some chemistry and therapeutics, while here and there throughout the volume even the dosage of individual drugs is given. Furthermore, we are hurried from the thyroid, the parathyroid, and the pituitary glands to some studies in digestion and absorption, from here we hastily garner some facts about blood pressure, but in a few minutes are thrust into the interesting mazes of the hemorrhagic diathesis. So we go through various subjects, uric acid, diabetes, and chloroform poisoning for example, while in the last two chapters we lightly jump, figuratively speaking, from cerebral localization to cutaneous anesthetics.

Written in this disjointed way, the book will never claim recognition as a book of reference, the subjects are for the most part dwelt upon in a too superficial and elementary manner. We find, however, that the author has published a most interesting and entertaining volume if we consider each chapter as a pleasing essay on the physiology of a certain subject with its application to practical medicine. He has taken care to sift the known from the unknown, the recognized and indisputable facts from the conjectures and theories of the various physiological problems as yet unsolved or but incompletely unravelled.

J. H. M., JR.

---

JUCKENDE HAUTLEIDEN. By DR. S. JESSNER, Sanitätsrat. Fourth revised edition; Pp. 120. Würzburg: Curt Kabitzsch.

THE author has endeavored to cover the entire domain of pruritic conditions in the short space of 120 pages. Itching conditions without an outbreak upon the skin are discussed in some detail; the various physiological or pathological changes are cited as a cause, particularly, for the universal cases of pruritus. The more

localized cases of pruritus, bath pruritus, pruritus hiemalis, and pruritus of the genitalia are cited. Particular attention is given to urticaria, the prurigo of Hebra, scabies, and pediculosis. Numerous prescriptions are mentioned as being efficacious for the pruritic conditions. Mitin is the base used for a large number of the external preparations.

F. C. K.

---

UEBER NEUROREZIDIVE NACH SALVARSAN UND NACH QUECKSILBER BEHANDLUNG. By DR. J. BENARIO. Pp. 195; 1 illustration. Munich: J. F. Lehmann.

BENARIO's monograph is at once timely and interesting. After Wechselsmann published his observations on Neurorezidives following salvarsan injections, a short search of hospital records unearthed 10 cases following mercurial treatment. One case only was found recorded in literature, although as early as 1610 Guarinori reported a case showing simultaneously a nerve lesion, primary sore, and exanthem.

In this book he reports 211 salvarsan and 121 other cases collected from Ehrlich's laboratory, correspondence, and from the literature. Analyzing his statistics, he incidentally notes preponderance among males, aged between twenty-five and forty years. Alcohol and, in a lesser degree, nicotine, predisposed to nerve lesions. Bakers and cooks also have more nerve involvement. Extra genital infections occurred in 12.3 per cent., chancre cephalique in 7 per cent. His numbers substantiate earlier observations of frequent brain involvement in cases of face chancre. Knorr first observed the association of nerve lesion and papular eruption. In this list 60.7 per cent. of the cases had papular or papulopustular exanthems. The Herxheimer reaction was present in 16 cases. Headaches were a prodromal symptom of rezidive in 50 cases and concomitant phenomena in 58 cases.

A detailed table of variations in manner and kind of treatment is added, with the conclusion that residues do not occur if the dose is sufficiently large or repeated within a short interval. The neurorezidive is an inflammatory focus occurring along the course of one or more cranial nerves. Three theories for these foci have been advanced: (1) A direct toxic injury to the nerve by the drug; (2) an indirect injury to the nerve, causing a place of lessened resistance where the colonization of the treponema takes place; (3) the escape of some treponema from the action of the drug and their subsequent growth in a practically new medium.

The pathology of syphilis itself is not entirely cleared up. The spirochetes have been found in the blood stream, but have a marked predilection for the lymph vessels, an explanation of the early

involvement of the lymph glands and the preponderance of lesions at the base of the brain. Recent writers believe the spirochetes proceed in the perivascular lymph spaces of the bloodvessels and of the pia. In the diseased vessel wall the organisms and lymphocytes are found, confined at first to the adventitia and media; later, also in the intima. The lymphocytic infiltration of the brain membranes shows itself in the lymphocytosis of the spinal fluid, a condition that persists after the disappearance of all symptoms.

In studying the 194 cases under the two modes of treatment, namely, mercury and salvarsan, he found that the same nerves are affected and in about the same order of frequency. This close agreement speaks most strongly against a neurotoxic action of salvarsan, and Benario thinks that this and the microscopic pathological picture prove that it is a true syphilitic process. He bases this belief upon (1) the long interval between the injection and nervous manifestation (one to four months); (2) the type of pathological process; (3) the fact that no rezidive occurs in non-syphilitics treated with salvarsan; (4) that in cases with already existing brain syphilis neurorezidives are not observed; and (5) neurorezidives recover under salvarsan.

The book touches fully and with a wealth of detail on the more important facts relating to this phase of syphilis. He urges more careful attention to changes in special sense organs in the early stage of syphilis, more energetic treatment, and control of treatment by the results of the Wassermann reaction and lumbar puncture. The long list of cases are tiring and the detailed treatment of each nerve lesion could be shortened with advantage.

E. P. C. W.

OPHTHALMIC YEAR BOOK FOR 1911. Edited by EDWARD JACKSON, M.D., THEODORE B. SCHNEIDEMAN, M.D., and WILLIAM ZENTMAYER, M.D. Pp. 455; 31 illustrations. Denver: Herrick Book and Stationery Company.

THE eighth volume of the *Ophthalmic Year Book* well illustrates the enormous increase in ophthalmic literature during the last eight years. The first volume in 1904 contained 260 pages whereas the present volume contains 455 pages with references to almost three thousand journal articles. The first 14 pages are devoted to biographic notices and then follows a digest of the literature classified as in the previous volumes. In the text, heavy-faced type has been used for the names of authors and the editors have returned to the previous custom of giving the page, in the various journals, on which any particular article may be found. In a volume of this character, these changes add much to the convenience of the reader.

Undoubtedly all subscribers to the Year-book have heard with much regret that its publication has been suspended, although to quote Dr. Jackson, "the purpose is not abandoned." It is hoped that the near future will find it re-established along lines where its publication may be resumed under conditions less arduous and more advantageous for its editors, for since its inception it has been a profitable convenience to those ophthalmologists interested in the literature in their particular branch of medicine. T. B. H.

---

FOURTH SCIENTIFIC REPORT OF THE INVESTIGATIONS OF THE IMPERIAL CANCER RESEARCH FUND. By DR. E. F. BASHFORD, General Superintendent of Research and Director of the Laboratory. Pp. 223; 63 plates; numerous charts and tables. London: Taylor & Francis.

THIS volume consists of three papers, preceded by a most interesting introduction by Dr. Bashford. The first paper on "Spontaneous Tumors in Mice," by M. Haaland, treats of a large number of spontaneous tumors of mice observed since the *Third Scientific Report* was prepared. "These tumors consist of carcinomas and sarcomas occurring in a variety of sites other than the mamma and are considered from clinical, pathological, histological, and experimental standpoints." From this study the writer believes he has produced evidence of possible local causes of tumor formation and lays considerable stress on local irritation as an etiological factor. The second paper on "Cancerous Ancestry and the Incidence of Cancer in Mice," by Dr. J. A. Murray, deals with breeding experiments with mice of known ancestry. The conclusion is drawn that female mice in whose ancestry cancer of the mamma has occurred not further back than the grandmothers, are distinctly more likely to develop the disease spontaneously in this organ than those in whose ancestry the history of cancer is remote. The third paper on "The Behavior of Tumor Cells during Propagation," by E. F. Bashford, is a general survey of the observations made on the tumors observed in the laboratory during a period of eight years and yields "evidence of the validity of the conclusion that the cancer cell is a biological modification of the normal cell."

All the studies show the thoroughness and attention to detail which characterize the work in this laboratory. The studies are presented *in extenso*, are splendidly illustrated with microphotographs and microscopical drawings, and are rendered additionally clear with charts, tables, and diagrams. The book is of great value to those occupying themselves with cancer as a biological problem and the introduction is of such a character as to make the studies available for the less intensively specialized reader. H. T. K



CLINICAL LECTURES ON THE ACUTE ABDOMEN. By WILLIAM HENRY BATTLE, F.R.C.S.; Surgeon to St. Thomas' Hospital, and Joint Lecturer on Systematic Surgery in the Medical School, etc. Pp. 107; 10 illustrations. New York: William Wood & Co. 1911.

THE author has grouped together in this small book of a clear and interesting review of those acute and dangerous conditions which are always of great importance to the general practitioner and surgeon. The term "acute abdomen," however, is open to the criticism that only pathological conditions of the abdomen can be acute, not the abdomen itself. A fair indication of the value of the book is found in the various affections discussed: Acute appendicitis and its complications; perforations of the gastrointestinal tract; acute intestinal obstruction; acute pyosalpinx and its complications; extra-uterine gestation; acute hemorrhagic pancreatitis; acute dilatation of the stomach; embolism and thrombosis of the mesenteric vessels; and infections of the gall-bladder with its complications. There is no attempt to enter into details in the discussion of the various conditions, but to present them as they occur in practice as surgical emergencies. As a whole, the work is lucid and practical, and will be of much value to any one who has to assume the responsibility involved in the care of these dangerous cases. It is not necessary to agree with the author in everything he says; for instance, that catgut should not be used at all in acute abdominal cases, or that the medical adviser should be so skilled in the recognition of the various aspects of appendicitis that he should be able to say definitely when immediate operation is "imperative."

T. T. T.

---

DENTAL ANESTHETICS. A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS. By WILFRED E. ALDERSON, M.D. (Durham), M.S., B.Hy., D.P.H., Honorary Physician, Newcastle-upon-Tyne Dispensary; Senior Honorary Anesthetist, Newcastle-upon-Tyne Dental Hospital, etc. Pp. 100. New York: William Wood and Company, 1911.

ALTHOUGH the title indicates that the book is one especially intended for dentists, yet it should be most useful also to the medical student and practitioner, as it gives in a concise and complete form the action, choice, and methods of administration of the various anesthetics in common use. The author agrees with American teaching in regard to the routine use of ether in preference to chloroform. The volume is completed by a chapter on analgesia or local anesthesia, by John Bolam, L.D.S., speaking more particularly of its application in dental operations. R. H. I.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College and Physician to the Jefferson Medical College Hospital, etc., assisted by LEIGHTON F. APPELMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. II, June, 1912. Pp. 391; 65 illustrations. Philadelphia and New York: Lea and Febiger.

THE June number of *Progressive Medicine* opens with a contribution of 32 pages by William B. Coley on hernia. In addition to the commoner forms of hernia rare varieties are discussed, especial attention being paid to diaphragmatic hernia.

General surgery of the abdomen is dealt with by John C. A. Gerster in an admirable article of 96 pages. He takes up a wide variety of subjects of which may be mentioned a careful review of Clairmont and Handek's monograph on the radiology of the stomach, which affords an excellent discussion of the diagnosis of gastric conditions, cecum mobile, the operative treatment of chronic intestinal stasis as advocated by Lane, a discussion of Heyde's noteworthy contribution on the etiology of the inflammation of the appendix, cholangitis, and acute pancreatitis.

The contribution on Gynecology by John G. Clark embraces 112 pages almost half of which are given over to a thorough discussion of cancer and fibroid tumor of the uterus. Among the other subjects to which he devotes considerable attention are: Pelvic inflammatory diseases, menstrual disorders, medical or non-operative treatment in gynecology, the ovary, the bladder, and ureters, and recent advances in the operative treatment of gynecological conditions.

One of the most interesting features of *Progressive Medicine* for a number of years has been Alfred Stengel's article on the blood, metabolic diseases, and diseases of the thyroid gland, nutrition, and lymphatic systems. In importance and careful preparation his present contribution compares favorably with those of previous years. Leukemia and pernicious anemia are dealt with at some length; hemophilia and the various blood dyscrasias including scurvy are next taken up; then, after discussing leukocytes and Banti's disease, considerable attention is given to diabetes mellitus, gout, obesity, and exophthalmic goitre.

In a short but well written article of 24 pages Edward Jackson takes up recent advances in ophthalmology. He considers his subject systematically under the following headings: Diseases of the conjunctiva, diseases of the uveal tract, glaucoma, the crystalline lens and vitreous, and the retina, optic nerve, and tracts.

G. M. P.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**A Test of Gastric Motility.**—I. BOAS (*Deutsch. med. Woch.*, 1912, xxxviii, 455), reviews briefly the methods of measuring gastric motility. No very satisfactory clinical method exists. He finds, however, that the results of Moritz, who showed that the human stomach is nearly empty one-half to three-fourths of an hour after drinking 500 c.c. of water, are substantially correct. There is ample experimental evidence to show that in dogs similar conditions exist. Boas utilizes this fact as the basis of his test; (1) because water which is drunk does not stimulate the secretion of gastric juice, at least, to any appreciable extent, and causes no pylorus reflex; (2) fluid which remains in the stomach is easily recovered; (3) the procedure is not complicated by layer-formation or sedimentation; (4) since relatively large quantities pass the pylorus in a short time, the determination of motility can be made within a half hour, even in pathological cases. With pure water there is one objection; it is impossible to be certain that all fluid remaining in the stomach has been completely removed. For this reason the addition of a dye is desirable. Boas selected chlorophyll. It is well adapted to the purpose, since it is absorbed neither from the stomach nor the intestines. The technique adopted is the following: The test is always performed on a fasting stomach. If the organ is not empty, it should be washed until the water comes away clear. The patient is then given 400 c.c. of water to which 20 drops of chlorophyll (concentrated aqueous solution) have been added. Thirty minutes after the patient has drunk this, the stomach tube is passed. With normal motility about 50 to 60 c.c. are recovered. To determine whether all of the residual water has

been obtained, more fluid is poured through the tube. For this purpose a 1 per cent. solution of soda is employed. If X represents the residue recovered, then  $400 - X$  c.c. of soda solution are poured through the tube and siphoned off. The quantity of chlorophyll in the wash water is then determined colorimetrically as follows: Prepare a stock solution of chlorophyll 1 to 400 and make dilutions of this of 0.5, 0.3, 0.2, 0.1 and 0.05. (The stock solution 1 to 400 corresponds to that which the patient drank). The wash water is filtered and the color intensity compared with the solutions prepared as above. If it is found, for example, that the green of the wash water corresponds with the chlorophyll solution 0.2, this means that 0.8 chlorophyll has passed through the pylorus in thirty minutes, or, expressed in percentage, 80 per cent. The patient should be instructed not to swallow saliva during the test, as it interferes with the quantitative determination of the chlorophyll. As the test solution is green and patients occasionally object to drinking it, Boas places it in green glasses. Boas has made observations on about one hundred and fifty patients with gastric disease and describes the results found in various conditions.

---

**Ehrlich's Aldehyde Reaction in Circulatory Diseases.**—A. JONASS (*Wien. klin. Woch.*, 1912, xxv, 375) has investigated the relationship between competence of the right heart and Ehrlich's aldehyde reaction. He finds that when there is insufficiency with consequent chronic passive congestion of the liver, the aldehyde reaction is positive. The positive reaction is, therefore, in a way indicative of the work done by the right heart in such cases. The reaction also becomes positive in asthma during the attacks, disappearing in the intervals.

---

**Experimental Eosinophilia after Intraperitoneal Injection of Protein and the Relation of Eosinophilia to Anaphylaxis.**—H. SCHLECHT (*Archiv f. exp. Path. u. Pharmacol.*, 1912, lxvii, 136), has investigated the eosinophilia seen in experiments with animals after injections with foreign protein and following anaphylactic shock. He finds that continued parenteral administration of foreign protein produces an eosinophilia in the blood of guinea-pigs and also in the peritoneal cavity. Cleavage products of proteins (as far as peptones) have the same effect, but amino-acids seem to be inert. Occasionally an increase of mast cells is seen. The eosinophilia is seen after a certain incubation period, during which eosinophile cells may be discovered to be in diminished quantity. The main source of the cells is the bone marrow; local production in the tissues may occur, but could not be established. Animals which have survived the anaphylactic shock react with a marked eosinophilia. Immune animals and those in an anti-anaphylactic state exhibit a further increase of the eosinophilia following renewed injection of the foreign protein. Eosinophilia is a favorable prognostic sign, both in experiment and in practice, in connection with anaphylaxis, since it is the expression on the part of the body of a reaction against toxic substances—a protective reaction. In this sense the post-infectious eosinophilia may also be interpreted. Schlecht points out the similarities between the conditions observed in anaphylactic experiments and in bronchial asthma, in both of which blood eosinophilia and local pulmonary eosinophilia are observed.

**Action of Salvarsan in Anthrax.**—BETTMANN and LAUBENHEIMER (*Deutsch. med. Woch.*, 1912, xxxviii, 349) report clinical and experimental results of the treatment of anthrax with salvarsan. Two patients presented themselves with typical anthrax infection. Each was given salvarsan 0.3 gm. intravenously and five days later a second dose of 0.4 gm. In each case recovery took place. The subsidence of the local signs was striking after forty-eight hours from the first injection. Within five days no bacilli were found in the pustules, and cultures were negative. Since anthrax usually terminates in recovery in human infections, it was decided to test the action of salvarsan experimentally. This was done with guinea-pigs. The result was that animals treated within five and a half hours after experimental infection almost always recovered, while controls, untreated, succumbed within two days. Animals which had recovered under salvarsan were re-inoculated with anthrax several weeks later, without treatment. They died promptly from the infection.

**Chemistry and Toxicology of Ascarides.**—F. FLURY (*Archiv f. exp. Path. u. Pharmacol.*, 1912, lxvii, 275), reports the results of painstaking and extensive researches into the chemistry and toxicology of Ascarides. Little is known of the biochemistry of the intestinal parasites and it is practically certain that the explanation of most, if not all, of the symptoms associated with such infections will not be entirely clear until such knowledge is obtained. Only the briefest partial summary of the present communication is possible. Flury's experiments were made on *Ascaris lumbricoides* and *Ascaris megalocephala*. On the relation of the body constituents and excrements of ascarides to the symptoms observed in the host, the following facts have been determined. Both in the body substances and in the excreta numerous substances are present which are capable of causing local irritation, hyperemia, inflammation, and necrosis. Most important in this connection are the volatile aldehydes of the fatty acids (which probably arise from the reduction of the corresponding acids), also the free volatile fatty acids of which the author isolated valerianic and butyric acids in considerable quantity and in smaller amounts, formic, acrylic, and propionic acids. Furthermore, local irritants, such as alcohols and esters of the ethyl-, butyl-, and amyl-series, were found. It is, no doubt, these substances which are largely responsible for the severe irritative symptoms, so well known to zoölogists, and for the hypersusceptibility which is not uncommon following repeated action of aldehydes; urticaria-like lesions are known to result from the vascular effects of esters of acids. In infected patients the prolonged action of such substances on the intestinal mucous membrane may well lead to symptoms. In addition to their irritative effects Flury has shown that the free acids, even in dilute solution, have a corrosive action which may injure the intestine. The digestive disturbances, which at times occur in ascaris infections may be due to the factors named. The absorption of substances from the intestine may be still more important. The conditions are present for the production of a chronic acidosis. Symptoms referable to the central nervous system, such as hallucinations, chorea, hysteria, epilepsy, delirium, etc. are explicable through chronic poisoning with aldehyde, especially atypically acting compounds of the amyl series.

Flury considers valerianic, formic, and acrylic acids particularly important in relation to nervous symptoms. The so-called meningitic form of *Ascaris* infection can be caused by any of several substances (alcohols, aldehydes, esters) acting on the meninges and producing increased intracranial tension from stimulation of the secretion of cerebrospinal fluid. Of nitrogenous compounds Flury has found a capillary poison which, when administered to dogs, causes fatal intestinal hemorrhage. The purin bases isolated may cause marked irritative effects in the central nervous system. The anemia seen at times in patients infected with *ascaris* may be due to the continued absorption of hemolytic substances. In this connection the most important are the unsaturated fatty acids and acrylic acid. Furthermore, injury to the blood may be due to reducing substances and those which inhibit coagulation. Additional toxins may be absorbed when the parasites die in the intestines and undergo decomposition.

---

**Deodorizing Excreta.**—A. CZERNY (*Berlin. klin. Woch.*, 1912, xlix, 450), refers to the disagreeableness of odors in the sick room. Not only the patient but the attendants as well are annoyed. In a large hospital ward the nuisance becomes even more serious. A simple deodorant for feces is highly desirable. At the suggestion of Uhlenhuth, Czerny tried antiformin. He finds that about 50 c.c. of 10 per cent. antiformin causes immediate and complete deodorization of fluid or soft stools. With formed feces the result is accomplished somewhat less quickly by pouring antiformin upon them, for the quantity used is not sufficient to cover the feces. Another use for the deodorant is its application to clothing, etc., repeatedly soiled by children. Even after the most thorough washing, some odor usually remains, but rinsing in 5 per cent. antiformin completely removes the odor without injury to the fabric. Again the method possesses an advantage in hospitals or dwellings which are unscreened, since the suppression of the odor greatly lessens the fly nuisance. Because of the low cost of antiformin (in Germany) the method may be widely applied.

---

**Leukocytic Inclusions in Scarlatina.**—M. KRETSCHMER (*Berlin. klin. Woch.*, 1912, xlix, 499), confirms the findings of Döhle who recently reported inclusions in the polynuclear neutrophile cells in scarlet fever. Kretschmer has found Manson's stain the most satisfactory for the purpose. A stock solution of 2 gm. methylene blue dissolved in 100 c.c. of boiling 5 per cent. borax solution is prepared. The blood smears are fixed in methyl alcohol, or in other ways, and are stained with a dilution of the stock solution, which should be transparent when held to the light. Stain 10 to 30 seconds, wash, dry, and mount. Red blood cells are light green to greenish blue, nuclei of leukocytes dark blue with reddish tint, and the inclusions are usually a somewhat paler blue, while the proplasm of the white blood cells is practically unstained. The inclusions vary in number from one to six. The form is not uniform; round or oval bodies the size of cocci, at times placed close together, appear, or crescent-shaped bodies with round or pointed ends are seen. They are invisible in the fresh specimen or with dark field illumination. Kretschmer has found these inclusions in the neutrophilic cells of 30 consecutive cases of scarlatina without exception.

From the beginning of the infection, even before the eruption appears, they are present in the great majority of cells, so that with the leukocytosis, which is usually present, there is no difficulty in finding them. They persist till the fourth day and may be found as late as the twenty-eighth day following the onset. With recrudescence of fever the bodies do not reappear in the blood. Kretschmer has been able to observe only 2 cases before the eruptions occurred. In one, the bodies were present in a number of the white cells the day preceding the eruption, in the other they appeared with the eruption. A new-born infant whose mother became ill with scarlatina a few days after its birth, escaped infection; in the mother's blood the inclusions were present, in the infant's absent. In several instances where the eruption was atypical, the presence of the inclusions settled the diagnosis. In other diseases Döhle found similar inclusions in only 3 instances—1 case of pneumonia and 2 of carcinoma. Kretschmer has examined 70 other individuals, 20 of whom were normal, and found inclusions in 4—1 case of pneumonia with suppurating cervical glands and 2 cases of diphtheria with streptococcus empyema and 1 of tuberculosis. In the 3 septic cases, he thinks it possible that scarlatina played a part in the etiology, but in a streptococcus septicæmia, no inclusions were found. He has observed only 2 anginas, one follicular tonsilitis and one Vincent's angina; neither showed inclusions. The inclusions bid fair to be of great significance in the differential diagnosis of exanthemata, Kretschmer believes.

**The Establishment of *Treponema Pallidum* as the Causative Agent of Syphilis, and the Cultural Differentiation between this Organism and Certain Morphologically Allied Spirochetæ.**—HIDEYO NOGUCHI (*Canadian Med. Assoc. Jour.*, 1912, iv, 269) reports that to establish an etiological relationship between an organism and the morbid process associated with it, Koch has postulated that the organism must be found constantly in sufficiently large numbers, that it must not be found in other diseases, and that it must be capable of producing similar pathological changes, when introduced into a suitable host in pure culture, as it does in the disease of which it is supposed to be the cause. In addition at present, immunity, anaphylaxis, and allergy have been proved to be essential factors in the determination of an organism as cause of a given disease. Noguchi gives the history of the investigations in morphology, animal inoculation, and for growth in pure culture, which have established *Treponema pallidum* as the cause of syphilis. Culturally *Treponema pallidum* shows strict anaërobiosis, requires fresh sterile animal or human tissue and serum in the media, does not produce coagulation or a putrefactive odor. The spirochetes grow by longitudinal division. They differ from the microdentium, a morphologically similar organism, by the facts that the latter grows more easily, is less anaërobic, produces a putrefactive odor, and after several weeks in fluid culture may produce a loose coagulation. In order to use the pure culture of *Treponema pallidum* for advancing knowledge of syphilis, immunity, and anaphylaxis must be considered. Noguchi found an allergic state of the skin to be present in almost every case of the tertiary stage, and in a large percentage of cases of latent and hereditary disease. By introducing a small quantity of a devitalized pure culture of pallida into the epidermis in such, a reaction is

produced comparable to Von Pirquet's tuberculin for tuberculosis. Noguchi has called this the luetin test. Noguchi believes that this reaction has its own sphere, being of prognostic value since it does not develop until the allergic state of the skin appears, indicating that the injection either is well borne, or is under better control due to treatment. Negative clinical symptoms or serological examinations do not show this. However, the significance of luetin will be demonstrated only through careful observations made by clinicians in different fields of medicine in the future.

---

## SURGERY

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**Operation for Perforated Stomach and Duodenal Ulcers.**—LAUPER (*Zentralbl. f. Chir.*, 1912, xxxix, 286) refers to Hoffmann's case reported by Offenberg in the *Zentralbl. f. Chir.*, 1911, No. 50 (abstracted in this journal, for March, p. 449) and Lauper reports his results with the same principles of treatment. About five years ago he had a case of ulcer at the pylorus with a perforation on the lesser curvature admitting the index finger, which came to operation fifteen hours after perforation with very marked symptoms of peritonitis. Closure with reliable sutures seemed to be impossible. A purse string suture going wide of the margins, succeeded only in approximating the edges somewhat, but did not completely close the perforation. A retrocolic gastro-enterostomy with a wide anastomotic opening, admitting three fingers, was performed and the site of the perforation was tamponned. The peritonitis was treated in the usual manner. After the removal of the tampon, at the end of a week, no stomach contents escaped and healing followed. In a case of perforation of an infiltrating cancer of the stomach with diffuse peritonitis, which was operated on about ten hours after perforation, closure of the perforation by suture was impossible and a simple strong tampon was depended on. This was allowed to remain in position for seven days. A gastro-enterostomy was not done, and all food by the mouth was withheld for several days. After removal of the tampon there was no escape of stomach contents from the opening, which later healed. In another case with perforation of a duodenal ulcer, operation was done fourteen hours after perforation. A long oval opening was found on the anterior surface of the duodenum,



about 4 cm. from the pylorus and admitting the index finger. After removing 2 to 5 mm. of the irregular, boggy margins, the opening was closed by a suture including the whole thickness of the bowel. A carefully placed turning in suture including one layer, was employed. The healing was good and there was no fever for a week, although the patient developed a complicating pneumonia. A gastro-enterostomy which was regarded as desirable was not done because the patient, an old man, was threatened with collapse during the operation. An intravenous, adrenalin-digalen-saline solution proved to be a life saving procedure. A long oval ulcer was excised from the anterior stomach wall and lesser curvature in a case of perforation of an apparently old, very callus ulcer, which came to operation on the third day after perforation. The excision was relatively simple with the application of two Doyen's clamps. The operation lasted over an hour and a half, too long for the severely collapsed patient. Death occurred two days later from peritonitis and exhaustion. The autopsy showed that the stomach contents did not escape, although the ulcer excision was not complete. In a case of pyloric ulcer in a man aged thirty-five years, admitted on the third day with a severe peritonitis and a history which pointed positively to a perforation of a gastric ulcer, operation showed the perforated ulcer at the pylorus on the anterior wall. A suture would have completely stenosed the pylorus and a gastro-enterostomy was indispensable. The perforation was covered over with a portion of the great omentum by a purse string suture and the site tamponned. The peritonitis was treated in the usual manner. The tampon was removed five days later but there was no escape of stomach contents. As Hoffmann maintained the treatment of perforated gastric and duodenal ulcers is not uniform but must be adapted to the individual case.

---

**Surgery of Horse-shoe Kidney.**—BOTEZ (*Jour. d' Urolog. Med. et Chir.*, 1912, i, 625) says that the horse-shoe kidney is an anomaly which is found in the proportion of 1 per cent. in 715 autopsies and 1 per cent. in 143 operations. Although the non-diseased horse-shoe kidney is an anomaly which in the majority of cases, does not reveal itself during life, yet it may at times be the cause of various physical or psychic troubles. The morbidity is great enough (16.25 per cent.) to show a predisposition to contract different diseases. All the diseases of normal kidneys have been observed in horse-shoe kidneys. A healthy horse-shoe kidney giving trouble reveals itself especially by functional symptoms; pain, digestive and nervous disturbances, which constitute a true syndrome, that of horse-shoe kidney. The physical symptoms and especially palpation can render the diagnosis more or less probable. When a horse-shoe kidney is diseased the diagnosis will be made especially by palpation and radiography. A principal characteristic will be the median position of the mass or of the calculus if present in the kidney. The treatment of a healthy horse-shoe kidney giving trouble is always operative. The ideal operation is a complete division of the isthmus, that is, the transformation of the two fused kidneys into two separate kidneys. The treatment of a diseased horse-shoe kidney is only that of the diseased kidney. Each part of the kidney can be exposed by an extraperitoneal, lumbar, incision.

Because of the depth of the lobes and its more abundant vascularization, any operation employed ought to be modified in its technique and sometimes in its indications. With some restrictions and modifications of technique all renal operations can be practised on a horse-shoe kidney.

---

**Hydrarthrosis in a Horse-shoe Kidney.**—GRÉGOIRE (*Jour. d' Urolog. Med. et Chir.*, 1912, i, 659) reports a case in which the symptoms were referred to the urinary tract and a rather voluminous tumor could be palpated in the right flank. Anteriorly near the median line a smaller mass was felt surmounting the large tumor. Operation was done through a right lateral incision. After freeing the peritoneum posteriorly, a large and slightly movable kidney was exposed. On continuing the separation of the peritoneum, it was found that the inferior pole of this kidney was continuous without interruption with the inferior pole of the left kidney, showing the presence of a horse-shoe kidney. In the concavity of the fused kidney was seen the second tumor which had been palpated before operation near the median line and which was formed by the markedly distended pelvis, prominent anteriorly. All the vessels of the renal pedicle were posterior to the pelvis. The ureter came from the internal border of the pelvis, and directed itself downward and posterior, in such a way as to produce a sharp curve at its upper extremity. The ureter was firmly adherent to the uniting pole of the kidney. It was freed and its direction rectified. Immediately the retention disappeared with great ease. The ureter was then fixed in good position by two or three fine, silk sutures to the capsule of the anterior surface of the horse-shoe kidney. The kidney was raised, slightly increasing the angle made at the origin of the ureter. The convex border was then fixed to the twelfth rib and abdominal wall by a few sutures. Healing was without incident. Three months later the patient was entirely well and had had no pain in the affected side since the operation.

---

**The Experimental Production of Basedow's Disease.**—KLOSE and LAMPE (*Zentralbl. f. Chir.*, 1912, xxxix, 641) say that in a previously published extensive work they have established that the intravenous introduction into dogs of very small quantities of the fluid pressed from an exophthalmic goitre can lead to the production of Basedow's disease, while large quantities of a similar fluid from the usual simple goitres will be without effect. They therefore regard this disease as a disthyroidism. Baruch's work supported the idea that it was a hyperthyroidism, because he produced what he regarded as the clinical picture, from intraperitoneal injections in different animals of crushed portions of simple and colloid goitres. He held that little or none of the substance producing the disease, is to be found in the fluid pressed from the gland. Klose and Lampe maintain that such fluids represent the concentrated cell contents and the classical form of biological experimental material. The material obtained from the crushing of the gland is a mixture of intact cells, which in an organism becomes effective only after the cell contents have been released by ferments. The resorption, therefore, is much slower than when the cell-free fluids are employed. The following objections are made against Baruch's

results: To be convincing the clinical results must be obtained after a single injection of the material employed as in their experiments. Baruch obtained the clinical picture described by him, usually after repeated injections.

---

**Orthopedic Resection of the Pelvis of the Kidney for Hydrarthrosis, with Intermittent Crises.**—GAYET (*Jour. d'Urolog. Med. et Chir.*, 1912, i, 625) says that the operation consists in removing a part of the pouch of the pelvis in order to bring the dimensions as much as possible to the normal. Albarran published the first case in 1898, although Kümmel had performed the operation in 1896, but did not publish the case until several years later. Gayet did the operation in 1910 with very good results. He was able to follow his case and very recently, two years after operation, he made a complete examination of the urinary tract. The patient had suffered in the right kidney for eight years, presenting for four years painful crises with renal distention, repeated once or twice each month. The treatment consisted in a nephropexy and orthopedic resection of the pelvis. At the examination more than two years later, no distention was found. The patient was completely relieved for five months, but for four months she has been suffering from slight pains in the two lumbar regions. the presence of a rectal ulceration and a certain degree of emaciation, makes one think of tuberculosis. But this is combatted by the negative inoculations, limpidity of the urine, and the absence of bacilli and albumin. The late result of the operation may be considered good, especially from the point of view of the regular emptying of the pelvis and the functional capacity of the kidney. According to Michel the operation has been done eight times, Gayet's making the ninth.

---

**Surgical Pathology of the Stomach and Duodenum.**—BINNIE (*Surg., Gynec., and Obst.*, 1912, xiv, 446) found that wounds of the stomach heal well; that the stomach is wonderfully tolerant of foreign bodies; that hemorrhages occur without demonstrable lesions; and that hemorrhage, erosion, and ulcers can be produced by toxins in the circulation. Binnie also observed that acids favor, but do not cause, ulceration in the stomach, duodenum, and jejunum. That local anemia (injections suprarenin) can produce ulcers; that stimulation and section of the vagus can produce ulceration; that in the latter the ulcers persist, provided that the musculature of the stomach is not impaired; and that retrograde embolism into the gastric veins can produce hemorrhage and ulcer of the stomach. The one common factor present in all the experiments or observations made regarding the incidence of *ulcus ventriculi* is vascular change or injury.

---

**Observation on the Radical Cure of Hernia.**—NASSAU (*Ann. of Surg.*, 1912, lv, 857), in discussing the choice of an anesthetic, says that in children up to the age of sixteen or seventeen years and in neurotic individuals, some form of general anesthesia is as yet the necessary evil. In young adults, in the aged, and in all strangulated herniæ, except in children, he believes that general anesthesia should be avoided as far as possible and follows the method of operating under local anesthesia as laid down by Mitchell. The infiltrating solution

is made in two strengths. The strong solution is made by dissolving a hypodermic tablet containing  $\frac{3}{4}$  grain of cocaine and  $\frac{1}{100}$  grain adrenalin in 50 c.c. of normal salt solution. The weak solution contains the same strength tablet in 100 c.c. of salt solution. These tablets should be sterilized in very small cotton stoppered vials with dry heat, raising the temperature gradually during one hour to 100° C. Only two tablets are sterilized in each vial and they should be placed in cotton to avoid contact with glass. After experimenting with various syringes the best has been found to be the Record of 2 c.c. capacity. The patient's general nervous sensibilities are usually less on edge if a hypodermic injection of  $\frac{1}{4}$  grain of morphine is administered a few moments before operation is begun. The essential points of the operation are: (1) Careful skin infiltration (strong solution); (2) perfect blocking of the iliohypogastric and ilioinguinal nerves (strong solution); (3) avoiding any unnecessary handling of tissues; (4) absolute prohibition as to gauze dissection; (5) forewarning patient that at this or that point some discomfort may be felt for a moment until a fresh infiltration with the weaker solution can be made. The post-operative course of a patient operated upon under infiltration anesthesia is so much more comfortable than with the use of ether that it is hard to institute comparisons.

---

**An Experimental Contribution to the Formation of Arterial Capillaries in the Kidneys.**—ISOBE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxiv, 821) conducted experiments on rabbits and dogs to determine the formation of arterial collateral branches after implantation of omentum into the nephrotomized kidneys and after surrounding the decapsulated kidneys with omentum. The normal and hilum collateral capillaries of the kidney are very inconsiderable, so that after ligation of the chief trunks of the hilum vessels, the whole kidney substance was destroyed, as a rule. Only exceptionally were isolated portions of the urinary canal and a few injected capillaries preserved in the subcortical zone, in the border region between the cortical and medullary substance, and in the region of the hilum. In the kidneys which were decapsulated and surrounded by omentum, the capsule collateral vessels were more distinctly developed than in the normal. After ligation of the renal artery, a number of atrophied urinary canals and numerous injected vessels in the cortex, were found preserved. No glomeruli were found injected. By nephrotomy and implantation of omentum, collateral anastomoses in a very considerable degree, were formed, although not in a sufficient degree to take the place of the vessels of the hilum entirely. In this way it was found that after ligation of the renal artery, on both sides of the implanted omentum, in a zone about 0.2 to 1.0 cm. wide, the kidney substance was preserved and in it numerous vessels were injected. Many urinary canals were preserved continuously from the glomeruli to the papillary ducts with many well injected glomeruli. The injection of the glomeruli and the preservation of the urinary canals in their whole length never were found in the kidneys surrounded by omentum. Much less effective was the simple nephrotomy, without omental implantation, since the kidney wound healed with a linear scar and no noteworthy vessel anastomoses. Therefore, in chronic interstitial nephritis, the preferable operation is the nephrotomy with implantation of omentum. If the

general condition of the patient is bad, the preferable method is the surrounding of the decapsulated and scarified or simply decapsulated kidney, surrounded with omentum. Isobe recommends as the best method of all; scarification, nephrotomy, omental implantation, and complete surrounding of the bared kidney with omentum.

**Duodeno-jejunal Occlusion as a Separate Condition.**—BIRCHER (*Zentralbl. f. Chir.*, 1912, xxxix, 843) says that in the last year he has had a few opportunities of observing, after the most varied operations, that much feared postoperative, acute dilatation of the stomach, which when untreated is surely fatal, but which with Schnitzler's treatment, by the employment of the knee-elbow position, washing out of the stomach, and the injection of hormonal, were cured. He has also observed 3 cases in which an exactly analogous clinical picture, occurred independently and spontaneously. In the first patient, who was suffering from uncontrollable vomiting after a dietetic error, a diagnosis of a high ileus from hernia, was made. At operation the stomach was found much distended. As soon as the stomach and transverse colon were elevated and the duodenum exposed, the latter was seen to be distended to the size of a man's arm, and the distention reached to the duodeno-jejunal flexure. From there down the jejunum and ileum were completely collapsed and empty. The occlusion at the flexure being removed by the finger, gas immediately passed into the jejunum with a rumbling sound and the distended duodenum collapsed. As a prophylactic measure, a posterior, retrocolic gastro-enterostomy was performed. The patient recovered and was relieved of all symptoms. In the second case, the patient was admitted to the hospital with a much distended abdomen and in an unconscious condition. The diagnosis of peritonitis from a perforated gastric ulcer was made, but operation showed the same picture as in the first case, except that it was complicated by a duodenal ulcer and gallstones. The origin of the condition is still not understood. Bircher has since seen 3 other cases and finds that the condition may follow a more chronic course, but with remissions from time to time of acute symptoms. Operation showed regularly the usual distended duodenum with a stomach of usual size, while the jejunum and ileum were completely collapsed.

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

**The Effects of Pressure Lowering Drugs and Therapeutic Measures on Systolic and Diastolic Pressure in Man.**—LAWRENCE (*Arch. of Int. Med.*, 1912, ix, 409) says that recent investigations indicate that

the pulse pressure is an important factor in determining the efficiency of the circulation and is of more value in prognosis than the systolic pressure. He conducted blood pressure estimations in 20 patients with permanent hypertension—chiefly cardio-renal cases—all showing a continued systolic pressure of 180 mm. or over—to determine the effects of various pressure lowering agents on the diastolic pressure. The systolic pressure was first taken at the point where the pulse first appeared at the wrist after complete obliteration and the diastolic pressure then ascertained by the auscultatory method. Lawrence gives the results of the observation in charts and tables in his article and draws a number of conclusions from his work. Reduction of systolic pressure by the use of nitrites, venesection, hot air, or electricity, is accompanied by a fall of diastolic pressure amounting, as a rule, to approximately one-half of the systolic fall. Such a reduction produces a coefficient of pressure more nearly approaching the normal than that prevailing in conditions of hypertension. Sodium nitrite reduces diastolic pressure more rapidly than the more complex compounds, thus causing a shorter initial diminution of pulse pressure than mannitol or erythrol. The effect on the pulse is more marked than that of the other drugs, the duration of its action is slightly less. None of the nitrite group is efficient for maintaining a pressure at a permanently lowered level as a tolerance is soon required, and increasing the dose is apt to cause unpleasant symptoms. Venesection has a more lasting effect in lowering the pressure than have any of the drugs used by Lawrence. The diastolic pressure is depressed longer than the systolic, the pulse pressure thus being increased. The effect of hot air baths, electric light baths, and high frequency currents is uncertain; a fall in pressure, if produced is transient. Vasotonin is not certain in its action and is not safe to use in cases showing marked hypertension, an increase of which might bring about untoward results. In each of the 5 cases, in which this agent was used, it caused a rise in both the systolic and diastolic pressures, in one instance accompanied by a severe anginal attack and in another by marked vertigo. He adds that in cases with permanent hypertension the effect on renal function of lowering the general pressure is an important and interesting point which will be discussed in a later paper.

---

**The Treatment of Scarlet Fever with Injections of Serum from Convalescents.**—REISS and JUNGMAUN (*Deutsch. Archiv f. klin. Med.*, 1912, cvi, 70) report 12 cases of severe scarlet fever treated by injections of blood serum obtained from patients convalescing from scarlet fever. They injected from 40 c.c. to 100 c.c. of mixed serum from several scarlet fever convalescents intravenously. The disease was unusually severe in each case treated and the authors attributed the marked improvement in the general condition of these patients entirely to the injection. The temperature dropped 3° C. in from nine to fourteen hours with a corresponding drop in the pulse rate. The treatment seemed to have no effect at all upon local lesions in the throat, lymph nodes, or joints. This fact is regarded by the authors as proof of the specific action of the serum, as fever and general condition improved so markedly, notwithstanding the persistence or a definite increase in local inflammatory processes. The fever terminated by crisis in 10 of

the cases treated by serum while this occurred in only 2 cases out of 200 not treated by the serum. The patients treated by the serum all convalesced more quickly than the untreated cases. The authors believe that this treatment must be applied early in the course of the disease to be effectual. The serum should be from convalescent cases at about the eighteenth to the twenty-fourth day of the disease. The mixed serum from at least 1 patient should be tested before injection by inoculation and for the Wassermann reaction. For the sake of convenience they put it in ampoules each containing 50 c.c. of the serum to which five drops of a 5 per cent. carbolic acid are added.

---

**The Secondary Effects of Harmonal.**—HESSE (*Deutsch. med. Woch.*, 1912, xxxviii, 643) reviews the literature on the use of harmonal and gives in detail a case where the intravenous injection of 20 c.c. of harmonal was followed by severe collapse. His warning is valuable in view of the fact that harmonal is being widely used in post operative cases where there is abdominal distention due to deficient intestinal peristalsis. Hesse believes that harmonal has a marked depressant action upon the blood pressure and he therefore recommends that the blood pressure should be ascertained in every patient before administering the remedy. If the blood pressure is low, it should be considered a contraindication to the use of harmonal. He also suggests that adrenalin should be administered at the same time with harmonal in order to guard against a possible fall in blood pressure. In the case reported by Hesse the injection of harmonal had the desired effect upon the bowels, but he would recommend harmonal only in the most urgent cases because of its marked depressing action upon the circulation.

---

**The Hypodermic Injections of Iron and Arsenic in Secondary Anemia.**—MUSSEY (*Boston Med. and Surg. Jour.*, 1912, clxvi, 775) reports a number of cases of secondary anemia treated by hypodermic injections of iron and arsenic. The hypodermic use of iron has been advocated particularly by Italian observers and the preparations used by them seem to be far better borne than similar preparations made in this country. Mussey tried a solution of ferric citrate made in this country but the results obtained by its use were very unsatisfactory. The injection of this ferric citrate solution in doses sufficiently large to give therapeutic results were painful and caused considerable local irritation. In a few cases attacks of vertigo, fainting, and vomiting followed the injections. Mussey then tried a combination of iron and arsenic of each 0.06 gram, and sodium glycerophosphate 0.10 gram dissolved in 1 c.c. of distilled water. The resultant solution is placed in small glass ampoules, sterilized, and is ready for instant injection. The solution is free from irritating qualities and may be injected into the muscles of the thigh or into the deltoid muscle. The injections were given, as a rule, twice a week, though in some cases as often as one a day was given for a short time. In several cases the injections were only given once a week. Mussey believes this method of procedure is entirely practical in office and dispensary work and that it is a valuable adjunct to the treatment of anemia, secondary to some relatively mild condition. He says that it affords a method of giving the drugs

in which the exact amount taken is accurately known, and that it does away with the annoying complications that frequently result from the administration of the drugs by mouth. Of 14 cases treated in this manner only 1 failed to improve promptly. He also notes the marked benefit derived from this treatment in a case of pernicious anemia where the hemaglobin rose from 19 per cent. to 68 per cent. and the number of red blood cells increased from 950,000 to 3,490,000.

---

**Neosalvarsan.**—SCHREIBER (*Münch. med. Woch.*, 1912, lix, 905) writes concerning neosalvarsan which is a product closely related to salvarsan but having a number of advantages over the older drug. It was prepared by Ehrlich and has been given by Schreiber about 1200 times to 230 patients with no untoward effects. Neosalvarsan is very readily soluble in water and the solutions for injections should be made just before using in freshly distilled water. The reaction of the solution is absolutely neutral and therefore does not require neutralization with normal soda solution. Neosalvarsan was found to be much less toxic in the experiments on animals, and therefore Schreiber believes that it can be given in larger doses than salvarsan. He also believes that it is at least as effective as salvarsan in its therapeutic action. Untoward by-effects were not observed as frequently as after salvarsan. Finally, neosalvarsan is more suitable for intramuscular injection than is salvarsan. When given intramuscularly neosalvarsan does not give rise to the burning pain caused by salvarsan nor does it cause dense infiltrations at the site of injection.

---

**By-effects of Harmonal.**—ROSENKRANTZ (*Münch. med. Woch.*, 1912, lix, 931) reports a case where symptoms resembling those of air embolism came on during the intravenous injection of 10 c.c. of harmonal. The injection was given two days after a second laparotomy to break up adhesions that had formed nineteen days after an appendectomy. The patient gasped for breath, complained that his head felt as if it were bursting, face was drawn, and eyes fixed. These symptoms gradually subsided but were very alarming at the time. About seven hours after the injection an enema was followed by the passage of a stool and considerable flatus.

---

**The Treatment of Acute Endocarditis due to Streptococcus Viridans.**—TOREY (*Münch. med. Woch.*, 1912, lix, 971) reports 2 cases of malignant endocarditis in which blood cultures showed the presence of streptococcus viridans. This organism produces a subacute but extremely fatal form of endocarditis. One of these cases recovered after the intravenous injection of salvarsan and the improvement seemed to Torey to be due to injections. Torey has tried a great variety of other methods of treatment in cases of this type without success, and, although in other similar cases salvarsan has not been successful, he believes that a trail of this remedy is justifiable in all cases of malignant endocarditis.

---

**The Serum Treatment of Typhoid Fever.**—LUDKE (*Münch. med. Woch.*, 1912, lix, 907) advocates a new serum treatment of typhoid fever that theoretically rests upon a rational basis. He describes his method



of preparing the serum, which has both anti-toxin and bactericidal properties and gives in detail animal experiments that seem to indicate that the serum has an antagonistic action toward typhoid bacillus infections. He reports his clinical observations in 29 cases of typhoid fever treated with this serum. No deaths occurred in this series of cases and complications seemed to be much less frequent than in cases not under this treatment but otherwise under similar conditions. The serum must be injected early in the course of the disease. It seemed to have the most pronounced beneficial effect when it was given before the twelfth day of the disease. The temperature came down rapidly by lysis and the patients were convalescent in a few days. When the serum was given in the later stages of the disease it was not so clearly manifest that the course of the disease was shortened although symptoms, particularly the fever, were often much improved. To be effectual the injections should preferably be intravenous or intramuscular, either a single large injection or several repeated injections of smaller amounts.

---

**Untoward By-effects of Harmonal.**—FRISCHBERG (*Münch. med. Woch.*, 1912, lix, 990) reports a case where the injection of 20 c.c. of harmonal was followed by marked symptoms of collapse. This patient had a severe chill, lasting thirty minutes, followed by a rise of temperature to 105.8° F. During the chill the pulse became feeble, the face was slightly cyanotic, and the patient complained of intense headache. The injection was given on the fourth day after an operation for chronic appendicitis because of enormous abdominal distention and obstipation. The harmonal injection was apparently very effectual, as the patient passed flatus during the chill, followed in a few hours by a copious bowel movement with relief to the abdominal distention.

---

**The Treatment of Tetanus with Magnesium Sulphate.**—PARKER (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1746) reports in detail 3 cases of severe tetanus successfully treated by subcutaneous injections of magnesium sulphate. Parker says that the dosage recommended for intraspinal injection is 1 c.c. of a 25 per cent. solution for every 20 pounds of body weight. The dosage used in the cases treated by Parker was much larger and no ill effects were observed. Two of these cases were acute and severe, not fulminant, but belonging to the class from which one would expect a high mortality. The prompt relaxation resulting after the injections certainly shows that magnesium sulphate is of value in the treatment of tetanus. It has no specific action, but by quieting the excessive muscular action it permits the patient to obtain more rest and to take food and thus tides him over while he is manufacturing his own antitoxin. Parker calls attention to the fact that there are some dangers in the use of magnesium sulphate, as it has been shown that it often produces toxic effects, chief among which are depression of respiratory and cardiac centres. It has recently been proved, by Joseph and Meltzer of the Rockefeller Institute, that physostigmin antagonizes the toxic respiratory depression sometimes caused by magnesium. Parker says that it is well to bear this in mind, as it may be the means of saving life.

## PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,  
OF PHILADELPHIA.

**The Use of Salvarsan in Hereditary Syphilis.**—EUG. AUDRONESCU (*Deutsch. med. Woch.*, 1912, xxxviii, 761) reports excellent results with salvarsan in the treatment of hereditary syphilis in infants and children. This remedy may be used indirectly by injecting it into the mother who nurses a syphilitic child, or directly, in which case the child is given the injection directly into its own tissues. Audronescu used the indirect method with the best results in three infants, aged three months, three and a half months, and one year and three months respectively. The adult dose was given the mother and within a short time an entire cure of the syphilitic lesions occurred in the first two children. The third child, with optic atrophy following pertussis, was unaffected by the salvarsan, the atrophy having probably no syphilitic origin. The direct injection of salvarsan in infants has been held by many to be too dangerous for routine use. Audronescu, however, used it in 6 consecutive cases, with excellent results in 4 of them. The age of the children varied from two weeks to four and a half years. The dosage varied according to age, from 0.02 gram to 0.12 gram of salvarsan. Three of the cases were completely cured, one was greatly improved, one with hydrocephalus, icterus, and nephritis was unimproved. The last case, an infant aged two weeks, with a bullous eruption and superficial abscesses, was given 0.02 gram salvarsan as it was not thought possible it could recover. The treatment resulted in a surprising and marked improvement in the child's condition. Audronescu considers these cases very significant as showing the harmlessness of the direct injection method in children and also the remarkable curative effects. He believes that salvarsan should always be tried out in children with hereditary lues as it offers often the only possibility of cure. The usual treatment with mercury either by intermuscular injection, or inunction, or by mouth had no effect whatever on the cases noted above.

**The Treatment of Acute Spastic Bronchitis in Early Childhood.**—F. GÖPPERT (*Berlin. klin. Woch.*, 1912, xlix, 791) defines spastic bronchitis as a symptom complex similar to the asthma of later life. Von Comby refers to it as asthma in infancy. Czerny defines spastic bronchitis as a typical manifestation of the exudative diathesis. All the cases seen by Göppert have shown marked evidences of exudative diathesis. After a slight irritation of the upper air passages for several days the attack begins suddenly with sharp dyspnea and inflation of the lungs. The child exhibits intense restlessness and often cries out continually in suffocated tones. At the moment of onset the child becomes cold and deathly pale. The skin becomes cyanotic only in

children under four months of age. Every inspiration is labored and the expression is one of terror. The body temperature is variable, being sometimes high and again normal. After twenty-four to forty-eight hours the attack subsides leaving a bronchitis more or less severe which usually causes no serious trouble in children aged over six months. There exists in this condition, as in asthma, a apasm of the bronchial musculature, constriction of the superficial bloodvessels, and dilatation of the vessels of the splanchnic system. The first indication in treatment is to quiet the intense restlessness. Göppert, until recently, used chloral by bowel in small doses, which induces sleep, makes the respiration easier, and mitigates the condition when the child awakes. This treatment, however, is dangerous for children aged under four months, and in these cases Göppert first tried urethan in 0.5 gram doses with very good results. The subsequent trials with urethan showed that it was perfectly safe and very effective and so it supplanted the chloral in the treatment of these cases. Urethan is given by mouth in doses of 1 to 2 grams and causes a light sleep for one or two hours, followed by great improvement in the respiration, pallor, and distress, and occasionally by the entire disappearance of all the acute symptoms. This proves urethan to have an antispasmodic effect on the bronchial musculature. H. Meyer has also advised the use of urethan in the asthma of adults. In infants the dose must be sufficiently large. In the first three months the dose by mouth is 0.5 gram, 1.5 grams later on during the first year, and 2 grams for the second year of life. By rectum the dose is doubled. The dose may be repeated within forty-five minutes if necessary. These doses may be given with safety even though there be existing cardiac disease or bronchopneumonia. In the latter disease the condition at times becomes worse with increased restlessness as if spasm of the bronchial tubes here also played a part, although the restlessness is comparatively less in proportion to the respirations. In such conditions urethan has proved useful, and the degree of its effect tends to indicate whether the change for the worse is due to an element of bronchial spasm or to an anatomical progression of the disease.

---

**Studies in the Nutrition and Digestion of Infants.**—MAYNARD LADD (*Archives of Pediatrics*, 1912, xxix, 324) presents a clinical study of 82 cases of indigestion and malnutrition in infants, illustrating the results gained by adapting milk to individual requirements and the relative value of different types of food in substitute feeding. Much misconception of the American system of feeding is due to the rules for feeding normal infants given in text-books. These rules are no guide for the sick or badly nourished children in whom great variation in food requirements are found. Individual factors in every case modify the treatment and must be learned by observation and experimentation. Infantile atrophy or marasmus presents the most interesting of all difficult feeding cases. The majority of these cases are due to long-continued improper feeding. This may be due to an insufficient breast milk, an excessively strong, or an excessively weak modified milk. The overfed cases present the greatest difficulties from greater gastric intolerance. The statement that these cases will not tolerate

fat is often taken too literally, as a tolerance for fats may often be established by giving a very low fat percentage for a considerable time and gradually increasing it. Ladd emphasizes two essential points. One is that the percentage of one element pushed beyond the child's digestive ability unfavorably affects the digestion of all the other elements. The second is, that if one element, such as fat, is kept very low; much higher percentages of the other elements can be given. The digestibility of fat depends largely on the character of the carbohydrates and the exhibition of casein in an easily digestible form. The regulation of the quantity of each feeding, the intervals between, and the number of feedings are equally as important as the percentage composition. Ladd speaks highly of the "eiweismilch" of Finkelstein and Meyer who believe that the whey constituents of cow's milk cause its indigestibility. This mixture is given in cases of diarrhea with good results, but the inconvenience of its preparation is an objection. Much of the feeling against fats arises from three causes. These are too rapid increase of fat percentages, errors in the composition of formulæ, and insufficient quantities of lime to saponify the fatty acids. In Ladd's studies of 82 cases it was found that the addition of malt sugar to whey mixtures instead of milk sugar increases the rate of gain in weight. There were no deleterious effects from a prolonged use of whey elements. The use of malt preparations with barley exceeded in efficiency the plain cream mixtures and the plain whey mixtures with milk sugar. Superheating the milk in malt mixtures neither increased nor diminished the nutritive value. Many babies today are being underfed in fat percentages. The danger of scorbutus in superheated malt mixtures is minimized by the daily administration of small doses of orange juice.

---

**Inclusion Bodies in the Blood in Scarlet Fever.**—MATTHIAS NICOLL and ANNA WILLIAMS (*Archives of Pediatrics*, 1912, XXIX, 350) studied blood smears from 51 cases of scarlet fever and 25 control cases to test out the finding of inclusion bodies reported by Professor Dohle, of Kiel, and Martin Kretschmar, of Strassburg. Dohle, in 30 cases of scarlet fever blood, found inclusion bodies in the polymorphonuclear leukocytes in almost every case. By various staining methods they could easily be differentiated from the nuclear substance. Inclusion bodies were found in but 3 out of a large number of control cases. These were found in pneumonia and carcinoma. Kretschmar confirmed the findings of Dohle, having found the inclusion bodies in all of 30 cases examined. In 70 controls the bodies were found in only 3 cases—one of pneumonia and two in diphtheria with streptococcus empyema. Loeffler's or Mauson's stains are recommended as simple and efficient. Nicoll and Williams have to date studied blood smears from 51 cases of scarlet fever, finding the inclusion bodies described by Dohle in 45 cases, 6 cases failing to show them. The negative cases all had been ill for eight days or more. The positive cases had been ill less than a week, most of them less than four days. The inclusions consisted of small coccus and bacillary forms. In 24 control cases the bodies were found in 3 instances—1 of pneumonia, 1 of erysipelas, and 1 of measles with complications. The last case developed scarlatiniform rash and sore throat which was not diagnosticated as scarlet fever by the Board

of Health. Nicoll and Williams feel justified in believing that a blood examination in the first week of the disease will serve to differentiate scarlet fever from measles, German measles, and probably toxic eruptions. Differentiation from eruptions in sepsis, influenza, and tonsillitis must be determined by further study.

---

## O B S T E T R I C S

---

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

---

**The Diagnosis of the Pernicious Nausea of Pregnancy.**—INGRAHAM (*Jour. Amer. Med. Assoc.*, February 6, 1912), in a paper in which he reviews the recent literature of pernicious nausea, draws attention to the value of the thorough administration of dextrose by enemas as an indication of insufficient formation of urea. By using definite quantities of sugar alimentary glycosuria may be produced to determine the impairment of the liver and the disturbance of the glycogenic function. In operative interference in the toxemias of pregnancy, chloroform is dangerous and contraindicated. Extracts of the ductless glands should be given a thorough trial.

**The Needless Interruption of Maternal Nursing.**—KOFLIK (*Jour. Amer. Med. Assoc.*, January 13, 1912), in a paper on the "Nursing Infant," found that in 1007 infants, but 124 were entirely breast-fed, or 12 per cent.; 573, or 56 per cent., were breast and bottle fed babies while 28 per cent. were bottle-fed absolutely. Of those which were fed on the breast and on the bottle, 60 per cent. were put on the bottle at the fourth month, and the breast abandoned; and in only 20 per cent. of the breast-fed children was an attempt made from the start at mixed feeding, the practitioner abandoning the breast in the remaining cases, when for some reason the breast became insufficient. While it may frequently not be possible to have the infant entirely breast-fed, in these cases mixed feeding from the beginning will enable the mother to retain breast-feeding indefinitely, greatly to her advantage and the child's. Breast-feeding is too frequently abandoned for insufficient cause, and apparently mixed feeding is not considered as frequently as it should be.

**Icterus Neonatorum.**—HEIMANN (*Zeit. f. Geburts. u. Gynäk.*, 1911, Band-lxix, Heft 1) has studied the blood of infants in varying degrees of icterus to determine the cause of this condition. He finds that these children do not differ from other children in weight, temperature, or the character of the fecal discharges. He considers the condition of icterus to be one of the blood, and largely dependent upon the fact that the child does not assimilate sufficient albuminoid food.

When this condition is present it begins to digest its own tissues, and first its blood corpuscles. As these consist largely of nucleo-albumin, their dissolution leaves hemoglobin in solution, whose absorption occasions icterus. The duodenal catarrh present in these cases is merely an accompaniment and not an essential factor.

---

**Parturition during Adolescence.**—BONDY (*Zeit. f. Geburts. u. Gynäk.*, 1911, Band lxi, Heft 1) publishes an elaborate paper upon this subject, based upon the examination of 1000 primiparous patients aged between fourteen and twenty-seven years. His investigations show that the belief often expressed that a patient should not give birth to children until after the twentieth year, is not correct. His investigations would indicate that the most favorable period for the first parturition is between the eighteenth and twentieth years. So far as the performance of the physiological functions is concerned, the period would be between the eighteenth and twenty-third years. After this time the conditions become rapidly less favorable for mother and child. Between the ages of fourteen and seventeen years, successful parturition, with healthy children, is by no means uncommon, and this cannot be considered an unfavorable period for mother and child.

---

**Sugar in the Blood in Pregnancy, Labor, the Puerperal State, and Eclampsia.**—BENTHIN (*Zeit. f. Geburts. u. Gynäk.*, 1911, Band lxi, Heft 1) finds that the quantity of sugar in the blood increases during labor, especially in the expulsive period, afterward diminishing during the puerperal state. In some cases this increase is inconsiderable, while in others it is so noticeable as to constitute a marked phenomenon. In eclampsia a very large increase is observed. In labor muscular activity must be assigned as an essential cause, although no parallel can be drawn between the length of labor and the quantity of sugar. The violence of muscular contraction seems to be an important factor, which is demonstrable in cases of eclampsia, although here a toxic element is also present. Pregnant women with chronic nephritis and high pulse tension have an increased quantity of sugar, but other cases of nephritis often show less than the average. In patients observed by the writer, the pulse tension was not above 145 mm. Benthin describes the case of a patient coming under observation five weeks before labor, suffering from the nephritis of pregnancy. Early in the disease considerable improvement had followed a strict limitation of diet. On admission to hospital, the urine contained 0.75 per cent. of albumin and 0.063 per cent. of blood sugar. The second examination made thirteen hours before labor, after parturition had been in progress fourteen hours, and just after the patient had had one eclamptic convulsion, showed 12 per cent. albumin, and 0.097 per cent. blood sugar. On the eleventh day of the puerperal period the albumin was 2.5 per cent., the sugar 0.074 per cent. It was interesting to investigate the relation of the production of sugar to weak uterine contractions, uterine atony, and the convulsions of epilepsy, delirium tremens, and hysteria.

---

**The Differential Diagnosis of Pregnancy.**—OLSHAUSEN (*Zeit. f. Geburts. u. Gynäk.*, 1911, Band lxi, Heft 1) draws attention to the

difficulties in the differential diagnosis of pregnancy in the later months. He recalls the case of a patient fourteen years married, and not previously pregnant. Menstruation had been interrupted for several months. The abdomen increased rapidly in size and in weight, and in unfavorable sensations. On examination abdominal distention was greater than is normal at the end of gestation. Palpation was unsatisfactory. Under anesthesia three tumors of almost the same size could be made out in the abdomen and they were nearly ovoidal in shape. One was on the left side at the brim of the pelvis and apparently the pregnant uterus of between four and five months. The second was upon the right, just above the pelvis, while the lower extremity of this tumor filled the small pelvis. The third was entirely above the pelvis, and so high as to make pressure upon the diaphragm and produce dyspnea. In endeavoring to ascertain what these tumors were, the one in the pelvis from its consistence seemed to be a myoma, and apparently was subserous, with a pedicle. The one above this was diagnosed as a subserous myoma. Upon operation, the diagnosis was found to be correct, and both myomas were removed. Pregnancy succeeded to a successful termination. Olshausen also draws attention to the difficulties in diagnosis, occasioned by hydramnios. Ovarian tumor may also occasion confusion, especially in cases where the amniotic liquid increases very rapidly. The great tension of the abdominal wall and the walls of the uterus, makes the diagnosis very difficult. Fluctuation is present in hydramnios, and it may be impossible to palpate the child. Lateral flexion of the pregnant uterus may also occasion confusion. This is sometimes mistaken for hypertrophy of the supravaginal portion of the cervix, and is most often seen in multiparæ. In these cases it is difficult to determine whether one is dealing with a flexed uterus or with a para-uterine tumor. An especially valuable method of examination in these cases consists in following up the lateral border of the uterus by palpation from the vaginal portion of the cervix. Olshausen holds with the majority of writers, that uncomplicated retroflexion in many cases is a serious matter in pregnancy. This is proved by the disappearance of symptoms when the abnormal position is altered.

---

**Changes in the Symphysis and other Pelvic Joints in Parturient Patients.**—LOESCHKE (*Archiv f. Gynäk.* Band xlvi, Heft 3, 1912) reports in a well illustrated paper his studies of the changes in the symphysis and other pelvic joints occurring in parturient women. He believes that the normal symphysis gives a complete union. The static relations of the pelvis are different in children and in adults, as in the adult the symphysis is much more strongly bound together than in the child. When changes occur in the symphysis which weaken it as a joint, they are usually of two kinds: One is the degeneration of its tissues, and the other the result of traumatic injury. In all labors the symphysis is considerably stretched. During parturition the symphysis is practically a movable joint. In each succeeding pregnancy the pelvis should increase slightly in size from the development of new bony tissue. In multiparæ this can often be seen at the symphysis. In every pregnancy the tissues about the symphysis are enlarged through the development of bony material. In multiparæ

one often observes an increase in the bone extending for more than 2 cm. The same change undoubtedly occurs in the sacro-iliac joints, and this process must be considered as a part of the general hypertrophy of pregnancy.

---

**Pregnancy and Double Pyosalpinx.**—GRADL (*Zentralb. f. Gynäk.*, 1912, No. 17) reports the case of a woman, aged twenty-two years, who complained of symptoms often described in cases suffering from chronic pelvic inflammation. The uterus was anteflexed, somewhat enlarged, and softened. Gonococci were found in great numbers. At operation the right tube was as large as a hen's egg, and the left the size of a large walnut. Both were adherent to the rectum. The uterus was edematous and swollen. It seemed impossible to remove the tumors without injuring the intestine, and as both tumors were draining into the rectum they were allowed to remain, and the abdomen was closed. On the fifth day after operation the patient complained of pain and discharged bloody pus through the bowel. She gradually improved and left the hospital. She returned some time afterward three months pregnant and suffering from great pain, and urging that the uterus be emptied. This was declined, and the patient left the hospital. She again returned after labor with her child, stating that she had had spontaneous labor, but had suffered great pain. The third stage of labor and the puerperal period had been normal. The child was vigorous and showed no evidence of gonococcic infection. The interesting question arises as to how the ovum could have passed into the uterus in the presence of double pyosalpinx.

---

**Death of the Child from Rupture of the Umbilical Vessels during Labor.**—WILLIAMSON (*Jour. of Obst. and Gynec. of the British Empire*, April, 1912) reports the case of a patient in her second labor, with a generally contracted pelvis. The child was small and could easily be made to enter the pelvis. The child was delivered by forceps, the mother having had slight hemorrhage with each pain. It was pale and bloodless, and the heart was not beating. On examining the placenta it was found to be of the velamentous type. The first vessel to leave the placenta was the umbilical artery, which had ruptured two inches from the insertion of the cord. Where the artery left the cord a large vein entered, which passed across the amniotic sac between the amnion and the chorion, thence over the fetal surface of the placenta, and into the placental substance. The vein was an aberrant vessel. On examination, the vein was thrombosed, except at a point near its entrance to the main umbilical vein, where it contained no thrombus. This vein had been compressed during labor and it became distended with coagulated blood. It ran close to the opening in the membranes, through which the child was born, and was evidently a vasa prævia. It was compressed between the presenting part of the uterine wall near its entrance to the main umbilical vein, for in that place only it contained no thrombus. As a result of compression the vein became distended with coagulated blood. During the second stage of labor, the membranes not rupturing at once, pressure ruptured the chorion and the vessel was torn across. A similar specimen had been recently sent to the Museum of St. Bartholomew's Hospital.



The clinical history of this case was that when the membranes ruptured there was a gush of blood, and afterward a little escaped with each pain. The child was spontaneously born, and was white and bloodless. On examining the placenta, a branch of the umbilical vein was torn across at the site of rupture of the membranes. From this vein the child had bled to death. Knapp's interesting case of twins, where both children bled to death from the rupture of a single vein, is cited. During labor diagnosis may sometimes be made by feeling the pulsating vessels running across the presenting portion of the membranes. The bleeding may be mistaken for placenta prævia or accidental hemorrhage. The mother, however, shows no signs of bleeding. The prognosis for the child in these cases is bad and it usually perishes from asphyxia. In some cases it may be possible to rupture the membranes at a point where there are no vessels, but this requires considerable dilatation of the birth-canal. Williamson believes that if a diagnosis can be made early in labor, before the vessel is ruptured, that the child should be delivered by section. After rupture the child is so weak from hemorrhage that no radical operation can be performed.

---

**Ovarian Pregnancy.**—BANKS (*Jour. of Obst. and Gynec. of the British Empire*, April, 1912) reports the case of a multipara having a tender, doughy mass in Douglas' cul-de-sac to the right of the uterus. A diagnosis of extrauterine pregnancy was made, and at operation a small quantity of dark fluid blood was found free in the peritoneal cavity. The tumor comprised the ovary and tube, which was normal and free at both portions. Oöphorectomy was done, leaving a segment of ovary near the ovarian ligament. On examination, ovarian substance somewhat altered was found, with a darker spongy zone separating it from the membranes. The sac contained a fetus of eleven weeks. Microscopic study showed definite ovarian substance, with slight change in the vessels. Ovarian stroma could be traced to the point where the ovarian elements disappeared, the fibrillæ becoming compressed with a few thin-walled bloodvessels. A portion of the tumor was edematous and undoubtedly altered ovarian tissue, and in this trophoblastic masses could be identified. The chorion and amnion were found, the villi of the former being scanty and degenerated. A minute study of the specimen left no doubt but that it was an ovarian pregnancy.

---

**The Treatment of Puerperal Sepsis By Cultures of Lactic Bacilli.**—BRINDEAU (*Archiv. mensuelles l'Obstétrique*, March, 1912) reports his results in the treatment of 92 cases of the various forms of puerperal septic infection by cultures of the lactic bacillus. His results were favorable and indicated that this remedy increased the patient's leukocytosis and thus heightened her power of resistance. The remedy may be used freely, for it is not in itself poisonous. An active culture should be employed, the dose varying from 0.5 c.c. to 20 c.c. of milk containing the bacilli, at a temperature of 37° C. This method is successful in all cases of septic or putrid wounds about the genital tracts, and is especially valuable in vulvo-perineal ulcers following delivery. These surfaces cleaned rapidly after the treatment and were in good condition for a secondary operation for the repair of lacerations.

## GYNECOLOGY

---

 UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.  


---

**Ovarian Transplantation.**—An extremely interesting case of successful heterotransplantation of an ovary, with relief of very severe symptoms following an artificial menopause of two years' standing, is reported by ENGEL (*Berlin. klin. Woch.*, 1912, xlix, 985). The patient, a twenty-seven year old nullipara, had been subjected to an appendectomy and ventro-suspension in 1904, and to a double oöphorectomy in 1909. The latter operation was followed by very severe disturbances—hot flashes, vomiting, violent attacks of abdominal pain, sweats, profuse and irregular uterine hemorrhages. In 1910, therefore, a supra-vaginal hysterectomy was performed by Engel. After this the hemorrhages ceased, but the general condition of the patient grew steadily worse; to the physical were added psychic disturbances, going so far as threats of suicide. The patient was therefore readmitted to the hospital in 1911, and a healthy ovary, obtained from another woman at a myoma operation, was transplanted onto the anterior wall of the cervical stump. Only a short time elapsed between the two operations; during this time the ovary was kept in normal salt solution at body temperature. The operation was performed vaginally; a T-shaped incision was made in the anterior vaginal vault, the mucosa dissected to each side, and the ovary, split open, attached to the cervix with cat-gut sutures. The vaginal mucosa was then closed over the surface of the transplanted ovary. For eight days no effect whatever was noted; then the symptoms began to decrease in severity. By the seventh week after the operation the attacks of abdominal pain and sweats had entirely ceased; the other symptoms, such as hot flashes, etc., disappeared more gradually, but eventually entirely cleared up as well. The patient now enjoys the best of health, and has again taken up her work as a trained nurse. Engel believes that suggestion can be entirely eliminated as a factor in this case, as the first signs of improvement did not show themselves until eight days after the operation, and from then on progress was slow and gradual. For a time there was considerable watery discharge from the vagina, and grayish and whitish areas were to be seen on the surface of the ovary, but before the patient left the clinic the secretion had entirely disappeared, and the ovary appeared entirely healed.

---

**Is Laparotomy Indicated in Peritoneal Tuberculosis?**—HEIMANN (*Zeitsch. f. Geb. u. Gyn.*, 192, lxx, 159) says that although the Gynecologic Congress held in Munich in 1911 decided in favor of the operative therapy of peritoneal tuberculosis, his experience has led him to consider it inadvisable. His conclusions are based on the observation of 50 operated cases from the clinic of Zweifel (Leipzig) and Krönig

(Freiburg), 36 of these patients having been subsequently controlled for periods up to as long as ten years after operation. He divides his cases into two groups; (1) Those with practically no symptoms referable to peritoneal tuberculosis, the presence of this being discovered only at operation for sterility, retroversion, or some other condition. (2) Advanced cases, with marked symptoms, and objective findings in the lungs. All the patients in the first group were fully able to work before operation; of 18 whose fate could be ascertained from one-half to nine years later, only 7 were in possession of their full activity, while 4 had died, 2 of these as a direct result of the operation. These are results which cannot, as Heimann says, in any way be considered brilliant, especially when one considers that many of these patients would probably have undergone spontaneous cure if left alone. The results in 18 patients in the second class were even worse. Within one and a half years after operation 50 per cent. were dead, all either as a direct result of the operation, or from a general, progressive tuberculosis. Of the remaining 8, only 3 can be considered clinically cured, that is, able to do ordinary work. In most of the cases in this group the accompanying pulmonary tuberculosis was markedly and unfavorably influenced by the operation. Heimann concludes that in these cases the performance of a laparotomy has not fulfilled expectations; that the percentage of apparent cures stands in inverse ratio to the length of time after operation that cases are controlled; that the primary mortality is very high; and that in so many cases a lighting up of foci in the lungs or other organs results that laparotomy can no longer be considered a sovereign therapy for peritoneal tuberculosis. If it is to be employed at all, it should only be in cases of the serous, exudative form, and all severe cases, and all those with lung conditions or with fever should be excluded. Where operation becomes necessary to relieve pressure symptoms Heimann prefers to open the peritoneum through Douglas' pouch if possible, in order to avoid the possibility of a fecal fistula. If this is not possible, the smallest possible opening should be made through which the work to be done can be accomplished.

---

**Spontaneous Cure of Cancer.**—THEILHABER (*Deutsch. med. Woch.*, 1912, xxxviii, 1240) says that it can no longer be doubted that spontaneous cure of cancer does occasionally occur, about 200 such cases having been reported in the literature. He believes that a careful study of these may possibly throw some light on the principle by which this occurs, and may point out ways in which we can assist the process. He reports having observed recently 3 cases in which he believes a spontaneous cure of cancer had occurred. In all he had performed a complete hysterectomy for advanced malignancy, but had been unable to remove completely all the carcinomatous tissue. Contrary to his expectations, complete cure occurred in these patients, this having been demonstrated by recent examinations. The longest period elapsed since operation was seven years, the shortest four. Theilhaber further reports 2 cases which have strengthened him in his well-known belief that after treatment by hyperemia, and other means which tend to improve tissue nourishment, may prevent and even destroy recurrences. The first case was that of an old woman, aged fifty-six years, with advanced, ulcerative carcinoma of the cervix, and extensive parametrial

involvement. After curettage and cauterization, treatment with hot air, hot douches, and hot sitz-baths was begun. In addition, an injection of 0.05 gm. sod. cacodylate was given every other day; five injections of 4 c.c. of uterine extract were also administered. By the end of the fifth month the cervix was completely cicatrized, and all discharge had ceased. The patient gained 3 to 4 pounds a month, and now feels well and strong. The other case was that of a woman with advanced mammary carcinoma. Four weeks after operation marked edema of the arm and a hard swelling in the axilla had developed. These disappeared under the application of Bier's hyperemia, and the patient was lost sight of. Several weeks later the edema and lump had returned, but disappeared again after two months more of treatment. This was kept up some time longer, and the patient remains well after one and three-fourths years. Theilhaber believes that free hemorrhage at the time of operation tends to favor a good circulation in the tissue subsequently, and goes so far as to advise the withdrawal by venesection of 400 to 500 c.c. of blood after incomplete carcinoma operations in order to stimulate this.

---

**Treatment of Metritis.**—The treatment of chronic metritis and endometritis by the intra-uterine instillation of zinc chloride solution, originated some years ago by Prof. Delbet, is warmly advocated by two of his assistants, Mocquot and Moch (*Rev. de Chir.* 1912, xxxii, 779). For this purpose they employ a Braun syringe, with a very fine canula, so that the solution may flow back freely around it. After having determined with a sound the direction and extent of the uterine canal, the canula is inserted as far as it will go, and, gradually withdrawing it, 2 to 3 c.c. of a 5 per cent. cocaine or novocaine solution are injected, as the zinc solution causes considerable pain, unless the mucosa is thus anesthetized. After waiting five minutes, the canula is again introduced, and 1 to 2 c.c. of the zinc chloride solution injected in the same manner, the syringe being gradually rotated as the injection is being made. Since the canula is supplied with small lateral openings near the tip, this assures a thorough distribution of the solution. In rare cases, where the endometrial cavity is very large, 3 c.c. of solution are employed, but this amount should never be exceeded. Solutions of two strengths are used; for cases of "glandular" or parenchymatous metritis 30 per cent.; for the hemorrhagic form 40 per cent. After each injection the patient should remain lying down four or five hours, and may then return home. Mocquot and Moch consider this form of treatment far more efficacious than curettage, besides being much less of a procedure, never requiring a general anesthetic. While they have obtained marked benefit in all forms of metritis, some are, as a rule, more favorably influenced than others, especially the hemorrhagic forms, and cases following abortion. Where the adnexa are involved the results are, as a rule, less satisfactory. In about 4 per cent. of the cases thus treated very severe abdominal pains come on from one-quarter to one hour after the injection, and may last for several hours. It is impossible to tell beforehand in which cases these will occur; they may be accompanied by vomiting and syncopal attacks. Mocquot and Moch consider them due to contractions of the uterine muscle, and do not think that they have in any instance been brought on by a passage of

the solution into the tubes or peritoneal cavity, since the amount used is too small, and no pressure is employed. Although this method of treatment is employed, they state, almost daily in Delbet's clinic, no case of cervical atresia or other serious consequence has been observed, and in 3 cases pregnancy has occurred following cessation of treatment. As a rule, three or four, or even more injections are necessary, though in some instances one suffices. Enough time is allowed to elapse between treatments to permit the slough which forms to be discharged, this usually requiring about six or seven days.

---

## OPHTHALMOLOGY

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

DENVER, COLORADO,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,

PHILADELPHIA.

---

**Keratitis Punctata Subepithelialis.**—GRADLE (*Arch. of Ophthalm.*, xl, No. 5, 534) describes under the above term a form of keratitis of unknown etiology which occurs in females usually past the age of thirty. This keratitis occurs in the form of isolated grayish infiltrated-looking areas, lying under Bowman's membrane, with an intact superficial epithelium and characterized by subjective injection and photophobia. It occurs at varying intervals in either eye and is self-limited. It does not seem to be markedly affected by any known form of treatment.

**Pathology of Superficial Punctate Keratitis.**—From a study of this condition, VERHOEFF (*Arch. of Ophthalm.*, xl, No. 5, 486) comes to the following conclusions: Superficial punctate keratitis (Fuchs) is a form of neuropathic keratitis. The corneal lesions in this condition consist of slowly formed necrotic leukocytic infiltrates, seated beneath Bowman's membrane, and are due to the action of pyogenic diffusible toxic substances arising at nerve terminals. Clinical evidence indicates that the causal nerve lesion is in the ciliary ganglion, and that it is probably due to the elective action of a systemic toxin on certain of the ganglion cells therein. In this affection there sometimes occurs well-marked focal proliferation of the iris bloodvessels. This observation confirms the view that vascular nevi are neuropathic in origin, and suggests that certain angiomas arising later in life may have a similar origin. Disciform keratitis (Fuchs) is essentially of the same nature as superficial punctate keratitis, and is likewise neuropathic in origin. Traumatic relapsing keratitis is due to a state of irritability in the peripheral ganglion cells of the corneal nerves, resulting from intense stimulation of the nerve terminals.

**Treatment of the Early Stages of Senile Cataract.**—HENRY SMITH, I.M.S. (*Arch. of Ophthalm.*, July, 1912, p. 323) has obtained marked improvement in the vision in 8 cases of incipient senile cataract by subconjunctival injection of cyanide of mercury (20 minims of 1 in 4000). He considers that where vision has been reduced by half or less for distance, the case is amenable to treatment. If reduced over a half, there is little hope of improvement. The most promising cases are those in which distant vision has been reduced by about 30 per cent. or under. The pain induced by subconjunctival injection of mercury under cocaine is very severe for three or four hours. To control which the patient should be put lightly under chloroform and given at least one-third grain of morphine hypodermically. The eye looks exceedingly ugly for several days, though he has never seen any evil results. The improvement was first noticed on the third or fourth day and continued steadily for several months.

**Sclerectomy with Iridectomy in Chronic Glaucoma: Lagrange Operation.**—GRUENING (*Amer. Oph. Soc. reported in the Amer. Jour. of Ophthalm.*, July, 1912, p. 208) has performed this operation 21 times on patients, aged from twenty-three to eighty-two years, with intra-ocular tension varying from 35 to 55 mm. mercury. The tension was permanently reduced in all with decided improvement of vision in the majority. General anesthesia was required in most of the cases. When properly performed with a well applied conjunctival flap, the wound closes in a short time, the anterior chamber is restored, and the intraocular tension more permanently reduced than after a simple iridectomy.

**The Size of the Blind Spot and its Distance from the Point of Fixation in Emmetropia.**—VAN DER HOEVE (*Arch. Ophthalm.*, July, 1912, p. 350), from the investigation of 100 practically normal eyes, found the centre of the blind spot in the horizontal direction to be situated  $15^{\circ} 33' 47''$  from the point of fixation; in the vertical direction,  $1^{\circ} 40' 41''$  below. The horizontal diameter measures  $5^{\circ} 42' 55''$ ; the vertical diameter,  $7^{\circ} 26'$ ; and that it is surrounded by a zone relatively blind for white,  $\frac{1}{8}^{\circ}$  to  $\frac{1}{4}^{\circ}$ , and a zone relatively blind for colors  $\frac{1}{8}^{\circ}$  to  $\frac{3}{4}^{\circ}$ . If these figures are computed according to Landolt, the horizontal distance from the middle point of the fovea is  $4 +$  mm.; vertical distance,  $0.44 +$  mm.; disk diameter, 1.6125 mm.; disk height, 2.025 mm. The horizontal diameter of the papilla, 1.6125 mm. corresponds closely with a number of anatomical measurements. From these observations he believes that a horizontal diameter of the blind spot of  $7^{\circ}$  is too large, and one over  $6^{\circ}$  is suspicious and requires further investigation.

**Failure in Strabismus Operations.**—BIELSCHOWSKY (*Arch. Ophthalm.*, March, 1912, p. 134) makes a study of those exceptional causes of failure in the operative treatment of strabismus which occasionally occur. He urgently warns against precipitate operations; repeated examinations are requisite to determine possible deviations from the typical such as the dissociated character of the anomaly, the inconstancy of the angle, and its dependence upon physical and psychic conditions. As there are generally no subjective symptoms in ordinary

typical strabismus, search should be made for a neurosis when subject symptoms are present. The smaller the degree of strabismus and the more prominent the intensity of the subjective complaints, the greater conservatism should be exercised in regard to operation. If operation is insisted upon, the patient should be informed of the uncertainty of the result and of the possibility of the appearance and continuance of diplopia after operation. Finally, in spite of all precautions and care, there will be occasional unavoidable failures; the number will become smaller in proportion as the manifold factors in the etiology of strabismus, which form the basis for rational therapy, become more exactly defined.

---

**Dust-like Opacities in the Vitreous.**—STRAUB, before the Ophthalmological Society of the United Kingdom (*Amer. Jour. Ophthalm.*, February, 1912, p. 54) argued that inflammation of the vitreous body, for which he proposed the name "hyalitis," should be recognized as an independent affection. He injected into the vitreous body of the rabbit some pathogenic microbes. These microbes grew there and there only and attracted to the vitreous body serum and leukocytes, both of which latter were derived from the vessels of the ciliary body, but this did not constitute cyclitis. When pathogenic microbes were injected into the ciliary body itself, a real cyclitis, quite different from the hyalitis which occurred in the first experiment, was produced. As the two forms can be distinguished in the laboratory, the same distinction should also be made clinically. But this has not yet been done. The text-books state that the ciliary body pours out its exudate into the vitreous, but this is a mistake, as leukocytes do not allow themselves to be poured out. Metchnikoff has said that leukocytes only went where they were attracted by chemotactic bodies. When there were microbes in the vitreous those substances went toward the vitreous body; when microbes were in the ciliary body the leukocytes went to the ciliary body. He also felt sure that the vitreous body obtained no leukocytes from the cornea; in inflammation of the vitreous body the leukocytes come from the vitreous body.

---

## PATHOLOGY AND BACTERIOLOGY

---

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME

PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT;

SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

---

**Immunity Transmission from Mother to Offspring.**—It has been well established that passive transmission of antibodies from mother to offspring occurs, and to determine if this happens chiefly by way of the placenta or through the milk. L. W. FAMULENER (*Jour. of Infect. Diseases*, 1912, vol. x., No. 3) has undertaken some careful

experimentation, making use of hemolysins. It has been determined with all but certainty that hemolysins could be transmitted through the placenta to the fetus, but, on the other hand, many fetuses from abortions failed to show such hemolysins. From Famulener's work, as well as that of others, it appears that goats, highly immunized against sheep erythrocytes at a late period of gestation, transmit the specific antibodies to the suckling, and this not so much by the placenta as by the colostrum, much less so by the milk. Especially when immunization has been done during the period of gestation is the colostrum powerful in this regard, even more so than the blood serum. If the mother were immunized after the birth of the young, the sucklings failed to gain any demonstrable immunity. Even though the colostrum be rich, the milk may not be so, and often the hemolytic antibodies disappear rapidly from the latter. It must be stated, also, that a very high degree of immunity is necessary in the parent animal before appreciable amounts of antibodies are excreted by way of the milk.

---

#### A Suggested Explanation of the Apical Lesion in Tuberculosis.

—As a result of their work upon the relation of animal fat to tubercle bacillus fat, WM. CHARLES WHITE and A. MARION GAMMON (*Jour. of Med. Research*, June, 1912, vol. xxvi, No. 2) bring forward a reasonable suggestion of the frequency with which pulmonary tuberculosis attacks the apices of the lungs. By adding to culture media of various kinds fats sufficiently fluid to mix, it was found that the growth of the bacilli was greatly enhanced, even to hundreds of times as abundant a growth as that upon the simple media. Still more striking was the effect if the fat were acted upon by liver extract, so that split products of the fats were obtained. Leather had shown that the fats stored in the tissues in general are mobilized in the liver, and there prepared for use by other organs of the body. The liver-altered fat is poured into the inferior vena cava and thence into the pulmonary system. In the pulmonary artery, just before the division into the right and left branches, a great bag of blood is formed, "the blood in this portion must move with comparative slowness," and the light fatty compounds have a chance to rise in this blood, and at the highest point of this stream the vessel arises which supplies the apex of each upper lobe; so that the fat laden blood of the apex of the lung, with its qualities as a culture medium thus increased, tend to the greater liability of the apex to become the seat of infection.

---

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.



# CONTENTS

## ORIGINAL ARTICLES

- Defective Development from Arthritis in Early Life . . . . .** 469  
By GEORGE DOCK, M.D., Professor of Medicine in Washington University, St. Louis.
- The Metabolism and Successful Treatment of Chronic Joint Disease:  
A Preliminary Report . . . . .** 474  
By RALPH PEMBERTON, M.S., M.D., Physician to the Out-Patient Department, Presbyterian Hospital; Fellow of College of Physicians, etc., Philadelphia.
- The Healing of Gastric and Duodenal Ulcers with Bismuth . . . .** 495  
By CHARLES D. AARON, Sc.D., M.D., Professor of Gastro-enterology and Adjunct Professor of Dietetics in the Detroit College of Medicine; Consulting Gastro-enterologist to Harper Hospital, Detroit.
- Contribution to the Bacteriology of Peritonitis, with Special Reference  
to Primary Peritonitis . . . . .** 502  
By MORRIS FISHBEIN, M.D., Chicago.
- The Prognostic Significance of the Atropine Reaction in Cardiac  
Disease . . . . .** 514  
By JAMES E. TALLEY, M.D., Visiting Physician to the Presbyterian Hospital, Philadelphia.
- The Therapeutic Use of Tuberculin: A Working Hypothesis and Some  
Personal Observations . . . . .** 524  
By LAWRASON BROWN, M.D., Saranac Lake, New York.
- Rest Versus Climate in the Treatment of Pulmonary Tuberculosis .** 535  
By WILLIAM C. VOORSANGER, M.D., Visiting Physician to Mount Zion Hospital; Clinician to San Francisco Tuberculosis Clinic, San Francisco, California.
- Diabetes Mellitus and Tuberculosis . . . . .** 543  
By CHARLES M. MONTGOMERY, M.D., Instructor in Medicine in the University of Pennsylvania; Physician to the Henry Phipps Institute, University of Pennsylvania, and the White Haven Sanatorium.
- A Further Study of the Prognostic Value of Arneth's Leukocytic Blood  
Picture in Pulmonary Tuberculosis, Based upon 729 Counts in  
475 Patients . . . . .** 561  
By PAUL H. RINGER, A.B., M.D., Asheville, N. C.

<b>Changes in the Kidney Resulting from Tying the Ureter . . . . .</b>	<b>568</b>
By J. F. CORBETT, M.D., Associate Professor of Experimental Surgery, University of Minnesota.	
<b>Clinical Manifestations of Illuminating Gas Poisoning . . . . .</b>	<b>577</b>
By ROBERT S. McCOMBS, M.D., Associate in Medicine, Philadelphia Polyclinic and Assistant Physician to the Children's Hospital, Philadelphia.	

## REVIEWS

Surgical Operations. A Hand-book for Students and Practitioners. By Professor Friedrich Pels-Leusden . . . . .	585
Serum Diagnosis of Syphilis. By Hideyo Noguchi, M.D., M.Sc. . . . .	587
The Surgical Clinics of John B. Murphy, M.D., at Mercy Hospital, Chicago . . . . .	588
Nephritis. An Experimental and Critical Study of its Nature, Cause, and the Principles of its Relief. By Dr. Martin H. Fischer . . . . .	589
Die Erkennung der Psychopathischen Konatitutionen (Krankhaften Seelischen Veranlagungen) und die Öffentliche Fürsorge für Psychopathisch Veranlagte Kinder. By Professor Dr. Th. Ziehen . . . . .	591
Grundriss der hamatologischen Diagnostik und praktischen Blutuntersuchung; ein Leitfaden für Anfänger, Studierende und praktische Aerzte. By A. Pappenheim . . . . .	592
Recent Advances in Hematology. By Walter K. Hunter, M.D., D. Sc. . . . .	593
A Laboratory Guide in Bacteriology for the Use of Students, Teachers, and Practitioners. By Paul G. Heineman, Ph.D. . . . .	594

## PROGRESS OF MEDICAL SCIENCE

### MEDICINE

#### UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

The Phthalein Test. An Experimental and Clinical Study of Phenol-sulphonephthalein in Relation to Renal Function in Health and Disease . . . . .	595
A Method of Reducing Excessive Frequency of the Heart Beat by Means of Rhythmical Muscle Contractions Electrically Provoked . . . . .	596
Bacteriology and Pathology of the Tonsils with Especial Reference to Chronic, Renal, and Cardiac Lesions . . . . .	597
Abscess of the Lung and Liver. Simple Cure of a Chronic Case by the Upside-down Position . . . . .	597

The Blood Picture in Disease of the Glands of Internal Secretion . . . . .	598
A Source of Error in Nylander's Test for Glucose . . . . .	598
Diastase in Urine and Feces . . . . .	598
A New Method for the Determination of Total Nitrogen in Urine . . . . .	599
The Radiologic Examination of the Apices of the Lungs. The "Cough Phenomenon" . . . . .	600
On the Determination of Ammonia in Urine . . . . .	600

## SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

Further Experiences with the Treatment of Volkmann's Ischemic Paralysis and Contraction by the Method of Robert Jones . . . . .	601
Pyelotomy in Renal Calculi . . . . .	601
The Mode of Origin of Renal Tuberculosis . . . . .	602
A New Operation to Reestablish the Continuity of the Intestine after an Extensive Resection of the Sigmoid and Rectum . . . . .	602
The Operative Treatment of the Edema of Elephantiasis . . . . .	603
Supraclavicular Anesthetization of the Brachial Plexus . . . . .	604
Anesthesia of the Sciatic Nerve . . . . .	604
Investigations Concerning Surgical Methods of Treatment for Trigeminal Neuralgia . . . . .	605
End Results of Fracture of the Shaft of the Femur . . . . .	606

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

The Treatment of Diphtheria Infection by Means of Diphtheria Endotoxin . . . . .	607
Collapse Produced by Hormonal . . . . .	608
Report of a Case of Diabetes Insipidus with Marked Reduction in the Amount of Urine following Lumbar Puncture . . . . .	608
Splenic Anemia Treated with Salvarsan . . . . .	609
A Preliminary Report on Neosalvarsan, with Particular Reference to its Employment as an Intramuscular Injection . . . . .	609
The Influence of Theophyllin on Nitrogenous Excretion . . . . .	609
The Treatment of Syphilitic Diseases of the Nervous System by Salvarsan . . . . .	610
Five Years' Experience with the High Calory Diet in Typhoid Fever . . . . .	610
New Points of View in the Treatment of Diphtheria, Scarlet Fever, and Suppurative Processes . . . . .	611
The Use of Hexamethylenamin in the Affections of the Upper Respiratory Tract . . . . .	612
The Rapid Cure of Amebic Dysentery and Hepatitis by Hypodermic Injections of Soluble Salts of Emetine . . . . .	612

**OBSTETRICS**

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Fatal Cases following the Early Getting up in Parturient and Operative Cases . . . . .	613
The Technique of Suprasympyseal Cesarean Section . . . . .	613
The Development of Placenta Prævia . . . . .	613
Induction of Labor with the Modified De Ribes Bag . . . . .	614

**GYNECOLOGY**

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

X-ray Treatment of Gynecological Skin Affections . . . . .	616
Constipation and Headache in Women . . . . .	616
Relative Value of Various Substances Used as Douches . . . . .	617
Control of Hemorrhage in the Radical Operation for Carcinoma Uteri . . . . .	617
Histology of Pyosalpinx . . . . .	618

**HYGIENE AND PUBLIC HEALTH**

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND ARTHUR I. KENDALL, PH.D., DR. P.H.

Infectious Abortion and its Relation to Man . . . . .	619
Alimentary Anaphylaxis . . . . .	621

**PATHOLOGY AND BACTERIOLOGY**

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.

The Influence of Local Anemia upon the Action of Poisons and upon Infective Processes . . . . .	622
Vaccination with Sensitized Agents . . . . .	622
Some Facts about the Epidemiology of Tuberculosis . . . . .	623
The Process of Vital Staining . . . . .	623
A Comparative Study of Antibodies . . . . .	624

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

OCTOBER, 1912

---

ORIGINAL ARTICLES

---

DEFECTIVE DEVELOPMENT FROM ARTHRITIS IN EARLY  
LIFE.

BY GEORGE DOCK, M.D.,

PROFESSOR OF MEDICINE IN WASHINGTON UNIVERSITY, ST. LOUIS.

CHRONIC arthritis is rare in children, and this partly explains why many details are not as thoroughly known as is desirable. So, very few writers even mention the arrested development that might be expected from non-use or other causes in such cases. Osler quotes Still, who, in the first edition of Allbutt's *System*, volume iii, page 104, in describing the disease sometimes called after him, says: "In cases beginning before the second dentition there is often a marked arrest of bodily development; a child twelve and one-half years of age, in whom the disease began at four years of age, still had the appearance of a child six or seven."

Ollier first demonstrated that injury to epiphyseal cartilages causes retardation of long growth. Bidders and Vogt saw shortening after partial destruction of epiphyseal cartilages. J. Wolff showed that loss of growth in bones might occur far from seats of disease, that is, in the feet in coxitis. In contrast with these changes that seem not unexpected, Diamantberger and others have noted an enlargement of the great toes, which indicates a nutritional change of a less simple character.

I recently had a case under observation in which a youth aged twenty-four years, with a history of arthritis without heart lesion from the age of eleven, had slight general retardation as shown

by puerile figure and expression with defective development of the long bones and relative or absolute shortening of the bones of the extremities. I anticipated an opportunity for thorough Röntgenologic and other study of the bones and joints, but a terminal nephritis hastened the fatal end and an autopsy could not be obtained. It seems to me, however, that a report of the case may serve to direct attention to more thorough examinations in other cases, and that ultimately the processes involved may be explained.

ABSTRACT OF HISTORY. C. C.; single; aged twenty-four years; white; newsboy; admitted December 13, 1911, to Medical Clinic of Washington University Hospital; died January 7, 1912. No autopsy.

Abstract from St. Louis Children's Hospital records: First admission, September 22, 1900. "Two years ago patient had grip, which resulted in rheumatism." Physical examination shows greatly enlarged and painful joints, especially the small joints. Diagnosis: Arthritis deformans, chronic.

Second admission, October 1, 1901. Aged thirteen years. Diagnosis: Arthritis deformans. April 20, 1902, discharged; improved.

Present complaint "rheumatism."

Family History: Mother is living and well; aged forty years. Father died of rheumatism at thirty-one. Had three brothers and one sister, all in good health. One brother had an attack of rheumatism six years ago, but recovered completely.

Personal History: Never was sick until he was eleven years old. "Rheumatism in ankles from wet feet and exposure" was first trouble. Had diphtheria, measles, and scarlet fever at Children's Hospital when about fourteen years old. Had mumps and whooping cough at about the same time. Had measles last and seemed to be in much better health afterward than he had been before. "Rheumatism" has been constant, but was less severe after measles. Was out of Children's Hospital for a year and a half, then went to St. Luke's Hospital; was there nine months, and was much improved. Could get along very well with a cane when he left. Was not troubled much about walking for one year, then ankle was sprained and use of crutches begun. Has not been able to discard them since. Had gonorrhea four years ago; recovered in six weeks. Joints not affected at that time. He had occasional headache; nose has been partially obstructed since childhood. No pneumonia or bronchitis; no dyspnea; no pains in chest. No precordial pains or palpitation. Heart has never been said to be affected. Has had "indigestion" since two months ago. Patient thinks trouble is due to bad teeth; is sure it did not come from food. If too much liquid is taken vomiting occurs immediately after eating. Sometimes vomiting

does not occur for an hour, and sometimes in the morning previous supper is vomited. Vomitus always consists only of food taken at previous meal; often is bile-stained, but never has been stained with blood. If vomiting occurs several hours after eating the vomitus is scanty, a severe headache is always associated with vomiting. Headache stops in an hour after vomiting. Has no pain in stomach. Passes urine four to six times each night and once or twice during the day. No pain on urination. Large amount of urine of high color voided at night, but no great amount at one time. Urination is urgent and involuntary if closet is not reached at once. Muscles are very weak. Mental and nervous condition fairly good.

Uses small amount of coffee and tea, also small amount of beer and whisky; two or three drinks each week. Sleeps well, eats well. Has worked as newsboy on the street for several years.

Present disease, patient says, began in ankles after exposure and wet feet about thirteen years ago, when aged eleven years. Ankles were swollen and stiff for a week or two, then swelling moved up the muscles of both legs to the knees, which became swollen, hot, and red. Swelling spread upward until shoulders and arms were involved. Nearly all of the joints are stiff and the muscles are very small and weak. There is no continuous pain, but pains shoot from one joint to another. No pain in muscles. Throat and neck swollen for about two months. Never has been painful.

Present condition. December 13, 1911. Patient is a sparsely nourished young adult. Gums and mucous membranes pale. Pupils equal; react to light and accommodation. Ears and nose free of discharge. Marked swelling of tissue about neck and side of jaws, the normal lines being partially obliterated. No tenderness, nor can any glandular structures be palpated. No fluctuation.

Tongue coated, breath foul. Teeth in poor condition—pyorrhea alveolaris; no general glandular enlargement; nasal obstruction.

Thorax long, costal angle narrow, expansion slight; better over right front. Percussion note clear in front and in axillæ, auscultation negative. Heart: maximum impulse in fourth interspace, just inside the nipple line, 7.5 cm. from midsternal line. Heart action regular; sounds clear all over; slight accentuation of second pulmonic. Radial pulse regular, 84 to minute.

Abdomen natural looking; moves well; no masses or tenderness. Liver dulness begins above at bottom of fifth rib and ends one finger-breath below costal margin. Edge just palpable. Genitalia normal. Spleen not palpable.

Extremities. Marked atrophy in upper and lower extremities. There is fixation of right elbow and right wrist; marked thickening of middle phalangeal joints of both hands. On left, there is good motion in left elbow joint. There is ankylosis of both hip joints and partial ankylosis of both knee and ankle joints.

Blood, December 14, 1911: Red corpuscles, 5,200,000; leukocytes, 11,000; hemoglobin, 70; color index, 0.7.

Urine examination, December 12, 1911. Specific gravity, 1009; acid; cloudy; albumin, large amount; 1 per cent. by Esbach; sediment contains many hyaline, waxy, and cellular casts.

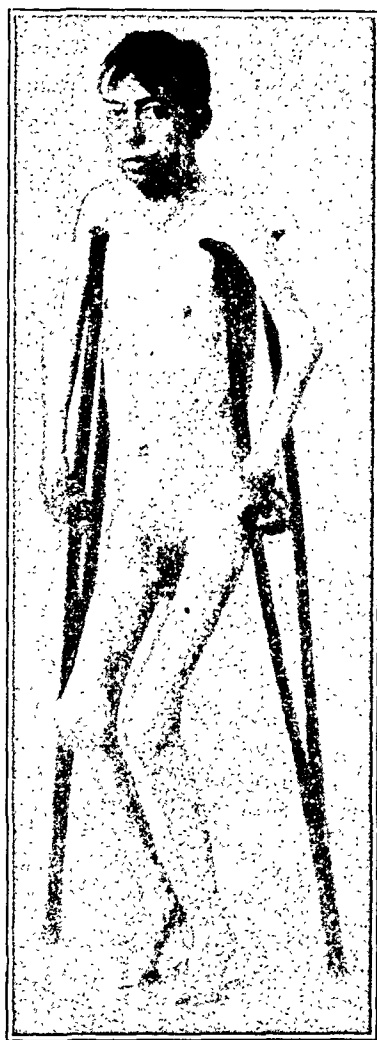


FIG. 1.—Photograph of patient showing his youthful appearance, the atrophy of the extremities, and the extent of the arthritis.

Note by Dr. Dock, December 15, 1911. Patient has an unusually youthful appearance; the arms and legs are poorly developed, the arms are very short (see measurements). The frame is juvenile, but the body hair and external genitals are well developed.

The appearance of the patient is best appreciated from the photograph, but a few of the measurements are given (*a*), with the measurements of a normal individual of about the same height



(b) and those from another case (c) of chronic arthritis, beginning at nine years of age with more marked fixation than the patient, but without special developmental defect.



FIG. 2.—Röntgenograph showing the changes in the bones and joints.

	A. cm.	B. cm.	C. cm.
Vertex to perineum . . . . .	84.0	98	75.0
Vertex to navel . . . . .	64.0	..	58.0
Clavicles . . . . .	12.0	..	12.5
Shoulder to elbow . . . . .	27.0	31	30.0
Elbow to wrist . . . . .	18.0	25	18.0
Wrist to end of middle finger . . . . .	16.25	18	18.0
Crest of ilium to trochanter . . . . .	15.0	15	13.0
Trochanter to knee . . . . .	36.5	40	35.0
Knee to external malleolus . . . . .	35.5	41	34.0
External malleolus to sole . . . . .	6.5	7	4.0
Length of foot . . . . .	19.0	27	21.6

The excretion of urine became smaller, the stomach became so intolerant of food that enemata were used, and they, too, soon became impossible to retain. Later the patient became comatose, and died next day, January 6, 1912.

The changes in the bones and joints can be realized fairly well from one of the many röntgenographs made by my colleague, Dr. R. D. Carman. The bones show rarefaction as is common in cases of chronic arthritis. Besides the erosion, cupping, and exostosis of the articulating ends, there is the not uncommon change in the shape of the heads of the bones, so that the heads of the humerus and femur, and the condyles of the femur and head of the tibia seem elongated. The shafts of the long bones are unusually thin and slender and the metacarpal bones and phalanges have cupping and broadening of the articular surfaces and narrowing of the shafts, somewhat suggestive of achondroplasia. It seems to me impossible to exclude the latter process, but I present the case without further comment.

---

## THE METABOLISM AND SUCCESSFUL TREATMENT OF CHRONIC JOINT DISEASE: A PRELIMINARY REPORT.

By RALPH PEMBERTON, M.S., M.D.,

PHYSICIAN TO THE OUT-PATIENT DEPARTMENT, PRESBYTERIAN HOSPITAL; FELLOW OF COLLEGE  
OF PHYSICIANS, ETC., PHILADELPHIA.

(From the Department of Clinical Chemistry, Presbyterian Hospital, Philadelphia.)

It is a familiar clinical fact that chronic joint troubles form one of the most frequent and rebellious of diseases. The application of laboratory methods to the diagnosis of the several varieties and the rational treatment dependent upon it have reduced many of these to categories which are fairly well understood and yield good results. Thus the tuberculous, Neisserian, and specific joints tell their own story, but after eliminating them there remains a large class in which but little progress has been made. This is the class grouped by various writers under the headings, rheumatoid arthritis, chronic articular rheumatism, arthritis deformans, and so on, conditions having in common an obscure or doubtful etiology and a prognosis for the most part unfavorable.

The activities of certain workers, particularly perhaps Goldthwaite and his collaborators in this field, have brought some order out of chaos, but it should be noted in passing, and with no credit to the internists and laboratory men, that it remained for orthopedists to suggest the simplest classifications and to practise the most rational therapy. It is due chiefly to the above men, for example, that we recognize in these obstinate cases the importance of a focus of infection in a tooth or tonsil, and that regulation of the diet along broad and intelligent lines is of the utmost value

in the undernourished and overfed. And again, we are now aware of the toxic possibilities incidental to a ptosed colon for which abdominal supports and operation have given much relief.

Grouping these cases as a whole, however, and eliminating them in turn from consideration, there remains a large and distressing number of cases which progress from bad to worse despite surgery, good hygiene, overfeeding, and underfeeding.

The principles of treatment as outlined above are now generally observed and practised by careful clinicians, but that they often fail is common knowledge. That the intestinal tract, however, is in some way or other connected with most of these last toxic arthritides is becoming more and more the belief of those who most frequently handle such conditions, but after what fashion it operates or what should be done for relief is not so clear.

In those instances where support for intestinal prolapse is not needed or fails, or where operation is not practicable or successful, there is often recourse to a consideration of diet, and it is partly with this phase of the subject that we wish now to concern ourselves.

More specific and detailed knowledge is obviously needed, and for lack of it, dietary control of these rebellious cases is practically renounced as impossible and not attempted.

The necessity of treating a number of sufferers from the conditions above indicated brought home to the author the desirability of some definite observations by clinical and laboratory methods from which an etiology and treatment could be deduced.

It is advised by many, for example, that in the dietary supervision incidental to good hygiene consideration should be had as to constipation, flatulence, the caloric need of the thin individual and the caloric surfeit of the fat individual, and that only the digestible foods should be eaten, that abundance of water should be ingested, and the like. At last analysis, however, these instructions are too generic, and in application generally fail of their purpose. Specifically stated, to feed these individuals with due regard to their nutritive needs and at the same time to avoid the element or elements which cause the joint disturbances, is the problem which presents.

Having found such a dietary regimen there would be offered thereby an opportunity for study of the processes active for good and evil which might yield facts of the utmost value. Why such a study has not been attempted before is not clear to the writer, since opportunity has at times presented in those cases which have yielded to the correction of intestinal ptoses.

Reference to the literature, however, indicates that while the contributions to chronic joint diseases have been legion, they have rarely been specifically along the lines indicated, and have rarely been accompanied by careful laboratory studies.

It has seemed evident for some time past to the writer that in

these joint conditions of intestinal origin several causative possibilities presented. (1) There is to be considered the activity of the intestinal flora *per se*, generally accepted for the most part as putrefactive, whose growth and by-products might cause absorbable toxic matter. (2) There is their action upon the ingested food to be considered, by virtue of which there may occur substances whose absorption might be causative of trouble. (3) There is the possibility of some defect in that disintegration and synthesis which gives rise to the "bau-steine," as a feature of pure physiological or pathological metabolism. How best to control the conditions of experiment to obtain a clue as to which possibility, if any, is operative, must be determined.

The writer has observed in a number of instances the remarkably beneficial effect of purgation and starvation upon the symptoms of certain joint cases, and the question is raised as to whether this be due to the absence of food decomposition and synthesis, to a diminution of intestinal bacterial activity, or to both. That the amount of food *per se* is an important factor apart from its relation to bacterial activity is indicated somewhat by the well-known favorable action of arsenic in these states, one action of which is probably to hasten the general metabolic processes. Another agent capable of this same action, though to a greater degree, is thyroid extract, whose gradual effect on nitrogenous exchange and the persistence of this after administration of the drug has ceased, are testified to by many observers.<sup>1</sup>

It is plain, therefore, that a great reduction of the food intake, active purgation, or the administration of agents which hasten the general body metabolism act beneficially on the symptoms of these conditions. The last mentioned agents, furthermore, are often beneficial even in conjunction with little or no reduction of the ingested food and may even stimulate the appetite to a greater consumption. If we apply the reasoning here suggested it would seem likely that there is a point at which one or all of the elements of food can be assimilated with satisfaction to the body needs and without detriment to any particular structure.

The lesson to be learned is in some respects like that taught by gout and diabetes, though the particular elements harmful in joint disease must yet be determined. An effort was made along these lines, beginning with the simplest of foods in order that the effect of their several component elements might more clearly be observed. Milk suggested itself at once, of course, as a basis for experimentation and our intention at first was to use whole milk. Experience with one case, however, in which "buttermilk" was successfully administered, seemed to urge further trial of it, and more systematic study of the results obtained. The question of the value, if any,

<sup>1</sup> Von Noorden, *Metabolism and Practice of Medicine*, iii, 991.

of introducing fermentative organisms into the intestinal tract by this means is still *sub judice*, though the observations of Herter and others have indicated the great importance of more work along this line.

There can be very little doubt, however, of the importance of learning the effects in these cases of reducing to a minimum the activity of the usual intestinal bacteria, and the simplest method of achieving this, in some part at least, has been shown to be by frequent movement of the bowels and by colonic lavage.

"Intestinal antiseptics" comes in here for very little consideration because of the discredit into which it has been brought by most observers and because drugs in any event introduce complicating factors. Whether, in this connection, by feeding fermentative organisms in large quantities in the form of buttermilk there can be produced an actual replacement of the customary intestinal flora is a problem whose terms and possibilities are not yet clear. It is worthy of study, however, and offers at least an hypothesis for development.

We desire here to report, therefore, (1) the results of treatment by these means in a series of chronic joint cases, and (2) the results of metabolic study of some of these individuals at certain periods of their progress. This report is to be interpreted, however, as purely preliminary and subject to the results of further study along the same lines. This is now in process, and only because of certain extraneous factors is it deemed advisable to report the results to date.

CASE I.—Mrs. M., aged sixty years, in comfortable circumstances and the mother of three healthy grown children, had been accustomed to robust health and rather unusual physical activity. She was first seen January 19, 1911, complaining of "rheumatism" or "gout" in her fingers and knee.

Physical examination revealed swelling and pain of all but the terminal finger joints of both hands, which had been growing progressively worse since the previous August. The second phalangeal joints had suffered the most, compelling her to remove her rings, though the dorsum of the hands was also puffy. Active and passive motion of these joints caused pain, and some of them had limitation of motion. The left knee was also tender on certain forcible palpation and gave considerable pain on walking, causing a limp and curtailing activity. The patient felt somewhat depressed but had no other subjective symptoms. She was rather heavily built, had a chronically slightly coated tongue (a feature common to at least two of her children), and a well audible mitral systolic murmur, together with a slight systolic murmur at the aortic cartilage. There was no noteworthy enlargement of the heart, and there had never been loss of compensation. The abdomen was rather large, flabby, and fat, with thin muscular walls, and in the

erect posture was somewhat pendulous. The patient objected to having an x-ray picture taken to ascertain the exact position of the stomach and large bowel, but the evidence was all in favor of some ptosis of both organs.

Her bowels had always been freely open at least twice daily, and often moved three times. Her blood pressure was 175 systolic and 75 diastolic, by auscultation. The blood and urine were negative, and a careful examination of the ears, nose, and throat by Dr. George Stout revealed no focus of infection. The accompanying picture (Fig. 1) shows the bony changes in the finger joints, characteristic of well-marked atrophic and hypertrophic arthritis. The patient had always had a good appetite and had eaten generously of everything, though not to excess, and was not in the habit of using alcohol in any form.

On January 27 she was instructed to eat meat but once a day, to stop her tea and coffee, to drink four glasses of water in addition to the fluid at meals, and was given daily four glasses of buttermilk prepared by artificial lactic acid fermentation.<sup>2</sup> Her usual diet was reduced over a period of about a week until the daily regimen was about as follows:

One glass of water on rising. Breakfast, consisting of a small amount of cereal, with cream and sugar, and one or two slices of well-done toast, with butter, hot drink (imitation cereal coffee, any of several varieties on the market) with cream and sugar if desired.

Between breakfast and lunch: Two glasses of "buttermilk" and one glass of water.

Lunch: Clear soup (or lettuce or spinach), one roast potato, toast (two slices), imitation coffee.

Between lunch and dinner: One glass of "buttermilk" and one glass of water.

Dinner: Clear soup (or twice a week a small amount of roast chicken, or twice a week 1 egg), toast or lettuce, imitation coffee, apple sauce.

Between dinner and bedtime: One glass of "buttermilk" and one glass of water.

Every afternoon about 5 P.M. the patient was given a simple enema and then high colonic lavage, with about  $1\frac{1}{2}$  quarts of normal salt solution, the washings being repeated until they came

<sup>2</sup> The milk used was that marketed by the Supplee milk establishment under the trade name "Fermillac." Its approximate composition is given by the manufacturer as 3.6 per cent. fat, 5 per cent. sugar, 3.2 per cent. proteid, 0.8 per cent. lactic acid. It is a fairly constant product, free from lumps, and for the most part of uniform consistency, though at times, probably from unduly prolonged fermentation, it is somewhat "coppery" and disagreeably acid. Patients were told to avoid it under these circumstances. They all professed to like milk prepared this way and seemed not to tire of it. There are several equally desirable artificially soured milk products on the Philadelphia market. They differ from buttermilk in that the fat is not removed.

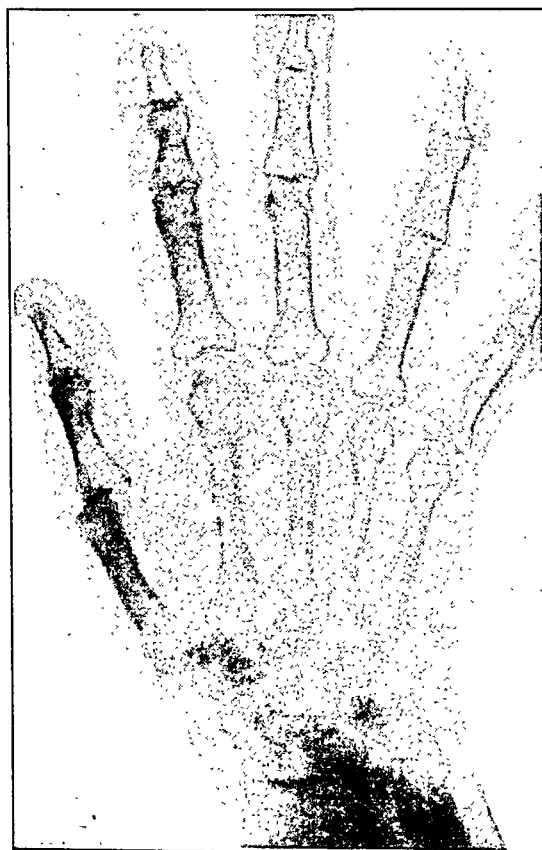
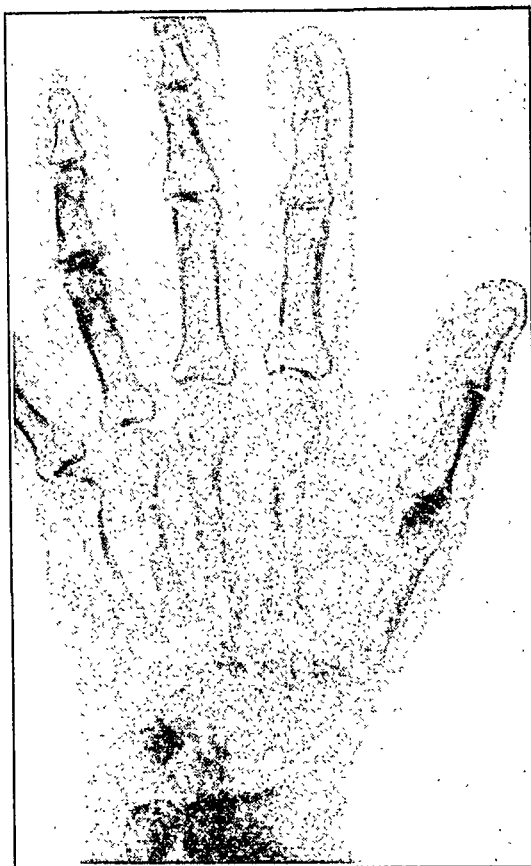


FIG. 1.—X-ray of hands of Case I, showing degree of joint involvement.

away fairly clear. Her bowels moved naturally in the morning. Later she preferred the injection in the morning about 10 o'clock, and was then given a glycerin-suppository at bedtime, always with result. The injections were given daily from January 30 to April 24, on alternate days from April 24 to May 6, thence every third day for two weeks, and then discontinued. Great care was exercised, of course, to avoid the slightest pain or local irritation in their administration.

The progress of her case is interesting and as follows, from notes taken at the time:

January 26. Treatment started. Weight, 167½ pounds.

February 2. Feels distinctly brighter and fingers are smaller.

February 8. Much better.

February 10. Weight, 163½ pounds. Pain in knee less.

February 14. Weight, 163½ pounds. Fingers are less swollen than at any time yet. A ring which could previously be removed with great difficulty or not at all now comes off with relative ease.

February 25. Weight, 164½ pounds. Condition good.

March 16. Weight, 162½. Blood pressure: 156 systolic, 75 diastolic, auscultatory. Before instituting treatment it was 175 systolic, and 75 diastolic.

April 29. Weight, 162. Blood pressure: 158 systolic, 85 diastolic. Practically free from subjective and objective symptoms.

Further notes on this point are unnecessary as her condition was excellent and remained so all summer, despite the fact that for two months she lived at hotels and allowed herself much liberty in her diet. For one month she stopped the buttermilk entirely, retaining, however, her increased fluid intake and eating with moderation of meats and starches. About four months later, however, she appeared again for treatment.

As the result of the excitement of Christmas and the visits of some friends, as well, perhaps, because of deliberate intent, she began to eat more freely of puddings, rice pudding especially, and the so-called "simple desserts." On January 28 she weighed 157 pounds 3 ounces, and presented distinct pain and swelling in the ring finger of the left hand. She had of her own accord renewed the "buttermilk" in October, and was taking in January four glasses daily. She was then advised to stop all meat and starches except zweibach, to increase the milk by two glasses daily, and to rest more. She developed three days later bronchitis, with slight fever, cough, and coryza, but at the same time her fingers improved.

On February 15 she was given a squab for lunch, and from then on her diet was increased until at the end of March it averaged as follows:

Breakfast: Cereal with cream and sugar, toast, imitation coffee, with cream and sugar.

Lunch: Spinach, toast, "coffee."



Dinner: Roast chicken, roast potato, toast, "demi-tasse" of "coffee."

In addition to the above she had her usual amount of "butter-milk," four glasses daily, as above described.

The patient was perfectly content with this diet. By this time she felt well and was free from all joint manifestations. A short but sharp diarrhea during the attack of bronchitis had pulled down her weight, which recovered somewhat, and stood on March 25 at 151½ pounds. By April 18, however, she expressed herself as having never felt better, weighed 154¼ pounds, and was taking a practically unrestricted diet of everything that came to table, with the exception of obviously indigestible articles like corn and griddle cakes; the "buttermilk" had been reduced to four glasses daily. This served to lessen her appetite at table and reduced consequently the amount which she would otherwise have eaten. Though previously a large eater of meat she was now satisfied with smaller amounts. It is interesting to note that at the time of her relapse she had increased her usual dietary by starches and sugars only, and had taken no more animal proteid of any kind. Upon reducing these again and with her return to health her tongue changed its character from being quite heavily furred and white to a nearly clear red. This excited her comment and was unique with her except for the periods of convalescence above mentioned.

Experience with this case determined the writer to pursue the subject in other individuals, more carefully and with laboratory methods.

The following represents the first attempt to that end.

CASE II.—John H., aged fifty-six years, a carpenter by trade, had suffered for five years past with increasing involvement of most of the fingers of both hands, both knees, especially the right, and the left foot. He also complained of stiffness and pain in his shoulders. His previous medical history was negative except for an attack of what resembled malaria and for the loss of one eye by accident eighteen years before. He had always been a great sufferer from constipation, and on occasion his bowels would not move for eight days. He denied alcoholic and venereal history, and was the father of several healthy children.

Examinations showed a spare man of middle height. Thorax and abdomen essentially negative, except for a palpable right kidney. Both hands showed extensive involvement, with marked deformity of the two middle fingers of the left hand. These were subluxated at the first phalangeal joint and presented distinct effusion.

The left knee was somewhat swollen, but the right foot was the part worst affected. It was swollen on the dorsal surface and pitted on pressure. There was no deformity of the toes, but pressure

below and anterior to the external malleolus, in fact most anywhere, gave much pain.

His weight was 115 pounds; blood pressure, 105 systolic and 52 diastolic. His blood count averaged: Red blood corpuscles, 3,130,000; leukocytes, 13,500 to 7000; hemoglobin, 70 per cent. An x-ray taken by means of bismuth showed that the stomach and colon were in the normal position and gave no clue as to the cause of his constipation.

This was deemed a good case in which not only to try the therapeutic effect of the diet described above, but also to attempt metabolic study, etc., of his condition before and after improvement, should this occur. To this end he was placed upon the following average diet:

December 27, 1911. Breakfast: Bread, 60 grams; two eggs, 89 grams; butter, 23 grams; milk, 256 c.c.; water, two glasses.

Dinner: Bread, 60 grams; rice, 41 grams; apple sauce, 127 grams; butter, 18 grams; milk, 256 c.c.; water, 1 glass.

Supper: Bread, 55 grams; two eggs, 90 grams; butter, 17.5 grams; milk, 256 c.c.

This diet varied slightly on different days according to the size and weight of the eggs, etc., but the amounts taken on the various days are omitted to save space. The sum total of ingested food appears in the accompanying tables.

Metabolic observations were conducted for four days on the following: Nitrogen of the urine, ammonia of the urine, creatinin of the urine, nitrogen of the feces, total sulphates of the urine, preformed sulphates of the urine, ethereal sulphates of the urine, total number of bacteria in the feces.

The methods employed were as follows: Nitrogen, Kjeldahl method; ammonia, Folin's method; creatinin, Folin's method.

The sulphates were precipitated with  $\text{BaCl}_2$  and calculated as  $\text{SO}_3$ .

The determination of the fecal bacteria was by counting, and will be discussed and described under Case III. The results of the latter in this case were unsatisfactory.

The figures obtained from the analysis in Case II were as follows:

	December 28	December 29	December 30	December 31
Nitrogen of urine . .	14.3942 grams	11.2 grams	8.624 grams	8.1984 grams
Ammonia of urine . .	.3745 grams	.1632 grams	.1904 grams	.3917 grams
Creatinin of urine . .	1.1984 grams	1.009 grams	1.0657 grams	.8872 grams
Ethereal sulphates . . . .		.1419 grams	.1579 grams	.3694 grams
Preformed sulphates . . . .		....	2.1249 grams	
Total sulphates . . . .		....	2.2828 grams	
Total nitrogen of the urine . . . . .				42.4166 grams
Total nitrogen of the feces . . . . .				2.6289 grams
Total nitrogen egested . . . . .				45.0455 grams

Total food ingested: Bread, 756 grams; eggs, 726.5 grams; butter, 219.5 grams; milk, 2834 c.c.; rice, 152 grams; apple sauce, 559 grams.

Total nitrogen ingested, 42.5695 grams. *Negative* nitrogen balance, 2.4760 grams. Comment on these figures will be made later.

This patient on January 2, 1912, was put upon a diet of "butter-milk," eight glasses in twenty-four hours, together with one egg at breakfast, one green vegetable at lunch, apple sauce at supper time. Later he was given one bowl of hot strained clear soup at lunch, as he suffered much from the cold weather and cold dietary. Because of his undernutrition it was thought well to push his diet as much as possible, and he was given on January 18, a total of ten glasses of "buttermilk." An effort was made to keep him out of doors in a chair, but he complained so from cold that this was discontinued. He was also given daily in the morning a simple enema, followed by high colonic lavage, with about two quarts of warm normal salt solution. In the early evening he was given a glycerin suppository, which was, however, invariably ineffectual. The enema usually gave some result, generally slight, and his bowels could not be said to move with much satisfaction.

The following notes show such progress as he made:

January 9. The swollen finger-joint (with effusion) shows slight improvement; foot no worse. Patient discouraged. Has been on diet about a week.

January 11. Slightly better. Finger-joint is smaller, with less effusion.

January 15. Distinctly better today for the first time. Swelling in foot is less. Complains of some pain in leg muscles.

January 16. Improves.

January 18. Still better. Right knee slightly swollen, probably from increased activity. Swelling of right leg below the knee has now practically all gone; took ten glasses of "buttermilk" in all today.

January 19. Both foot and knee better. Weight, 112½ pounds. Swelling of foot practically gone.

January 28. Slight swelling of foot today. Nails very blue after being out in the cold air. Two more glasses of "buttermilk" to be given daily.

January 30. Foot still swollen in afternoon and somewhat so at other times of day, but much less painful—in fact, almost free from pain.

From this date on there was very little appreciable change in the man's condition. The swelling of his finger had subsided not to return, his general health was better, the pain in his foot was so diminished that he could at times walk with relative ease, but the

edema of this one foot persisted, and he complained of pain in his shoulders, which kept him awake at night.

It had been the hope of the writer that at about this date or later another period of metabolic study could be undertaken, with the idea of comparing the various findings during improvement with those of the first period. The patient's condition, however, did not warrant the attempt, as he had not sufficiently improved. After a few weeks spent in the hospital he became restless, and was discharged at his own request.

In retrospect several errors can be detected in the attempt made with this case. The patient's general health had been so undermined, his constipation was of such an obstinate and long-standing nature, and he had such a marked anemia that a mistake was made in putting to the test with him any therapy without first relieving or modifying these conditions.

It was not desirable to cloud the issue by the simultaneous exhibition of iron, arsenic, etc., especially since metabolic observations were contemplated; but his anemia should have been actively treated, his constipation combated, and his weight increased if possible before the therapeutic test of his joint condition by means of dietary measures.

It is but just to say, furthermore, that this patient had been through half a dozen "cures" in this country and had tried many other treatments without avail. By the time that the arrest in his improvement became clearly evident, he grew restless, as mentioned, and desired to leave the hospital.

Furthermore, he required a degree of personal care in the way of massage and alcohol rubs to induce sleep, etc., which could hardly be administered with success in the public wards of a hospital, but he was of the opinion, judging by his own subjective experiences, that dietary regimen offered the only prospect of relief.

CASE III.—The next case studied was of greater interest possibly and gave much more encouraging results. The patient was a woman, aged thirty-seven years, who was deliberately chosen by the writer and asked to submit herself to treatment because of two facts: (1) She presented an unusually typical case of atrophic arthritis, of nine years' standing, in a young woman without other disturbances of health. (2) She had tried nearly every known treatment in a long series of hospital readmissions, during which she had been under the observation and care of at least nine careful clinicians. It was felt that success and study in her case would be especially satisfactory because of both the well-marked and progressive nature of her condition and the clear failure of other means of treatment. The essentials of her history, etc., were as follows:

Mrs. F., aged thirty-seven years, white, presented a negative

family history and had always been healthy until the onset of the present trouble. She had one healthy child, aged twelve years. In December, 1903, she was operated upon at the German Hospital, Philadelphia, for appendicitis by Dr. John B. Deaver, and made an uneventful recovery, except for long-continued drainage of the abdomen. Three months later, after returning to her duties, she noticed an ephemeral and shifting stiffness of various joints accompanied by transient swelling. One year later this had resulted in a chronic swelling and disability of the middle finger of her left hand. From this time she progressed steadily from bad to worse. Because of the arthritis she was admitted three times to the Hospital of the University of Pennsylvania for periods of six months, five weeks, and four months respectively, and while there had her tonsils removed and a rectocele repaired. She was also treated for a temporary cystitis of origin subsequent to her joint trouble. She was also admitted three times to St. Timothy's Hospital, Roxborough, for periods of three days, seven weeks, and two weeks respectively, where she had some further remaining tonsillar tissue removed. Apart from this she had been under private professional care on many occasions.

Aspirin usually gave her relief from pain, but for a few hours only, and the one other measure of any avail was thyroid extract. This was administered during one of her periods at the University Hospital, with relief for some months, when she relapsed worse than ever. A second administration of the same drug at St. Timothy's Hospital was not only without benefit to her joints, but seemed to make them worse, and resulted in tachycardia and other symptoms of hyperthyroidism.

On the present admission she presented swelling, subluxation, hyperextension, atrophy, pain, limitation of flexion, and ulnar deviation of the fingers of both hands. There was also marked involvement of the elbows and of both knees, especially the right, which was swollen and partially ankylosed in slight flexion. The left ankle also presented marked swelling and pain below and external to the external malleolus, which was hidden by the tumefaction. She could barely use her hands to write, and she could not bear her full weight on either knee or ankle, much less walk. She was confined to bed and required assistance in caring for herself even in bed.

Her physical examination was negative in other respects, except for considerable corpulence, chiefly of the past year's duration, a large relaxed abdomen, and the fact that an x-ray photograph by Dr. W. S. Newcomet showed marked ptosis of the transverse colon, with sharp angles at the hepatic and splenic flexures.

The x-ray photographs of her hands showed a well-marked atrophic arthritis, with relatively little deformity, but marked rarefaction of the heads of the bones and almost total absence of

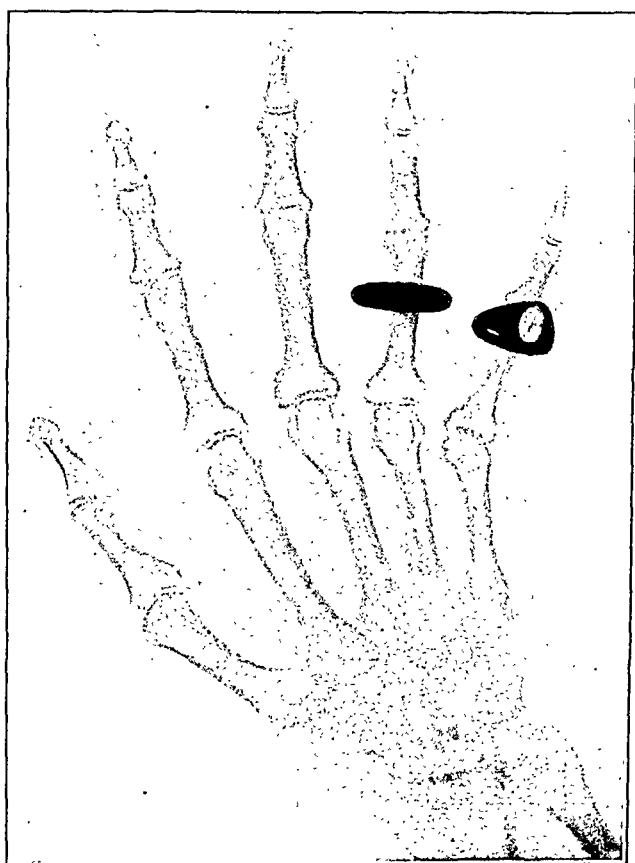


FIG. 2.—X-ray of hands of Case III, showing degree of joint involvement. The reproduction imperfectly illustrates the atrophic nature of the arthritis.

intra-articular cartilage. The plate of the right knee showed effusion and that of the foot some subluxation, in addition to the other characteristic phenomena of atrophic arthritis (Fig. 2).

The attempt was then made as with Case II, but here carried further, of placing the patient upon an average known diet, of no particular therapeutic value, in order to determine her metabolism while the diseased process was active. She was then placed upon the modified diet, and when improvement was sufficiently advanced another series of metabolic determinations was made. The results of these attempts follow.

On January 23, 1912, she was given the following average meals as the dietary of her first metabolic period and was kept in bed:

Breakfast: Bread, 47 grams; milk, 210 c.c.; one egg, 56.5 grams; water, 200 c.c.; butter, 13.5 grams.

Dinner: Bread, 27 grams; butter, 13.5 grams; milk, 300 c.c.; rice, 42 grams; sugar, 13 grams.

Supper: Bread, 42.5 grams; milk, 220 c.c.; one egg, 44.5 grams; water, 220 c.c.; butter, 13.5 grams.

The exact quantity of ingested food is tabulated later.

After she had been on this diet for three days her metabolism was studied with respect to the following: Nitrogen of the urine, ammonia of the urine, creatinin of the urine, ethereal sulphates of the urine, preformed sulphates of the urine, total sulphates of the urine, nitrogen of the feces, total number of fecal bacteria.

The figures follow:

	January 27	January 28	January 29	January 30
Quantity of urine . . .	1016 c.c.	1030 c.c.	940 c.c.	760 c.c.
Nitrogen of the urine . .	9.5756 grams	7.4466 grams	8.5660 grams	10.1360 grams
Ammonia of the urine . .	.3713 grams	.2570 grams	.2856 grams	.3536 grams
Creatinin of urine . . .	.9804 grams	.7896 grams	.9490 grams	1.0830 grams
Ethereal sulphates of urine . . . . .	.3673 grams	.3865 grams	.3557 grams	.4124 grams
Preformed sulphates of urine . . . . .	....	2.0262 grams	3.1260 grams	2.1913 grams
Total sulphates of urine . . . .	....	2.4127 grams	3.4817 grams	2.6037 grams
Total nitrogen of the urine . . . . .			35.7242 grams	
Total nitrogen of the feces . . . . .			1.1718 grams	
Total nitrogen egested . . . . .			36.8960 grams	

Total number of bacteria eliminated in four days by bowel, 373,750,000,000.

The total food ingested was as follows: Bread, 469 grams; butter, 160 grams; eggs, 405 grams; milk, 3530 c.c., rice, 108.4 grams; sugar, 52.5 grams; which yielded 36.266 grams nitrogen ingested. Negative nitrogen balance, 0.530 grams nitrogen. Her weight remained about 163 pounds.

On the completion of the above observations she was placed upon the following regimen:

Breakfast: Two glasses "buttermilk," one slice of toast and butter.

10.00 A.M. Enema of salt solution followed by colonic irrigation.

11.00 A.M. One glass "buttermilk."

12.30 P.M. Lunch of one glass "buttermilk," one green vegetable (spinach, lettuce, onions, cabbage).

3.00 P.M. One glass of "buttermilk."

5.00 P.M. Supper: Two glasses of "buttermilk," one slice toast and butter, one saucer apple sauce or stewed pears (not very sweet).

8.00 P.M. One glass of "buttermilk."

Water *ad libitum*, but she took very little.

The notes of her condition follow:

February 1. Diet started.

February 5. No indican, which had previously been abundant. Has a slight cold. No acetone. This was watched because of the reduction in the carbohydrates.

February 8. Hands seem much better. Gain of one-half pound in weight—now 159 pounds. Patient shows an unmistakable change since her new diet. Urine somewhat cloudy and shows white blood cells.

February 9. Hands slightly more tender in a few finger-joints, but no more swelling. No indican.

February 10. Doing well. Swelling of dorsum and of metacarpophalangeal articulations decreasing daily. Dimples begin to show over joint sites. Lost one pound.

February 12. Doing well.

February 13. Better. She is usually worse for one week prior to her menstrual period, but has escaped this time, though it is due tomorrow. This is her first experience of this. She says she moves better in bed and does not waken so stiff. Considerable indican today, probably referable to her period.

February 14. Menstruating. Slight soreness of hands. Possibly slight "cold" also.

February 22. No indican. Doing well.

February 27. Doing well and nearly free from pain on pressure over most joints or on motion of them. A ring which could not previously be removed without soap and water and much effort came off with relative ease for the first time.

February 28. Now getting the following average diet:

6.00 A.M. One glass of "buttermilk."

Breakfast: One glass of "buttermilk," toast, 26 grams; butter, 6 grams;

10.00 A.M. One glass of "buttermilk."

12.00 N. Dinner: Lettuce and salt, 24 grams; one glass of "buttermilk."

2.00 P.M. One glass of "buttermilk."



4.00 P.M. One glass of "buttermilk."

6.00 P.M. Supper: Apple sauce, 172 grams; toast, 24 grams; butter, 5 grams.

8.00 P.M. One glass of "buttermilk."

9.00 P.M. One glass of "buttermilk."

Daily enema and colonic lavage still being administered. Weight, 159 pounds.

The patient had by now progressed so far that the second period of metabolic study seemed advisable.

Her diet was therefore carefully weighed and measured, the results of which in terms of total ingested food for the period follow.

The figures obtained from a four days' metabolic study while she was still in bed are:

	February 29	March 1	March 2	March 3
Quantity of urine . . . . .	1930 c.c.	1650 c.c.	2130 c.c.	1350 c.c.
Nitrogen of urine . . . . .	7.7280 grams	7.2990 grams	8.2544 grams	6.5856 grams
Ammonia of urine . . . . .	.4896 grams	.3590 grams	.4488 grams	.3808 grams
Creatinin of urine . . . . .	.8728 grams	.8969 grams	.9548 grams	.7042 grams
Ethereal sulphates of urine . . . . .	.4884 grams	.4302 grams	.5251 grams	.3390 grams
Preformed sulphates of urine . . . . .	2.0558 grams	2.1611 grams	2.0795 grams	1.4565 grams
Total sulphates of urine . . . . .	2.5442 grams	2.5913 grams	2.6047 grams	1.7955 grams
Total nitrogen of the urine . . . . .				29.8670 grams
Total nitrogen of the feces . . . . .				2.8684 grams
Total nitrogen egested . . . . .				32.7354 grams

Total number of fecal bacteria eliminated in four days, 12,372,000,000,000.

Total food ingested: Toast, 201 grams; butter, 46 grams; "buttermilk" or "Fermillac," 8192 c.c.; lettuce, 150.25 grams; apple sauce, 607 grams; apples, 438 grams; which yielded *in toto* 41.3554 grams nitrogen.

There was therefore a *positive* nitrogen balance of 8.62 grams.

Subsequent notes are as follows:

March 4. Slight "cold" possibly. No fever. Right hand and wrist slightly sore. Allowed up. Weight, 159 pounds. Out in chair on piazza. Out every day on piazza. Her ankle is now much less painful, as is also her right knee. Wants to get up and go home.

March 29. Slight pains today in one hand and right elbow, due to approaching menstruation, possibly, which sometimes comes slightly ahead.

March 31. Menstruating. Diet increased to a total of one egg and fruit at breakfast, one slice of toast at each meal, one vegetable and soup at lunch, two green vegetables and stewed fruit at supper, with usual amount of "buttermilk."

April 4. Taking increased diet well and is apparently cured of

all active processes in her hands. The only painful parts are in the right knee, where the disability is possibly mechanical, and to a slight extent in the malleolus. This may also be mechanical, as the x-rays show a subluxation in the foot. Weight, 157 pounds.

April 26. Diet has been increased and the "buttermilk" reduced to only five glasses daily. Now taking chicken and a roast potato at lunch in addition to the egg at breakfast and green vegetables at supper; also has ice cream at times. Took fish from another patient once without orders, but it did not hurt her. Has had massage and stretching of her slightly contracted right leg, which is now becoming straighter. Is up and around the ward a little every day, and says that her foot is nearly or entirely free from pain. Menstruating today, but has no exacerbation of any symptoms, as occurred prior to treatment.

Enough has been said of the course of this case to show that to all intents and purposes her inflammatory arthritis at this point had subsided. In conjunction with the case first cited and the previous history of the present case the results leave no room for doubt as to the importance of these measures in at least some instances.

**METABOLIC FINDINGS.** The metabolic figures of Case II are given for what they are worth, but since no control observations could be made during marked improvement their value is minimized. They show nothing that could not be encountered in health, though the ethereal sulphates are conspicuously low as compared with the next case, and, indeed, are low for any individual who suffers much from constipation.

Metabolic observations on such cases during the activity of disease are not lacking, but data on the relative proportions of the various factors then and during convalescence are rare.

Turning now to Case III a review of the figures is more profitable. In the first metabolic period we find an output of ammonia which is just about in accord with what is usual in health, though verging on an output actually low.

The creatinin is about normal, as it also was in Period II, and can be dismissed from further notice. It is evident, so far as the creatinin output can be taken as an index of general muscular metabolism, that internal muscular metabolism *per se* plays no important role in this condition.

Considering next the ethereal sulphates we find rather high values, which might be expected *a priori* perhaps, though they are not excessive. It is interesting to note in connection with the ethereal sulphates here and in the next period that "Keffir" has been mentioned in doses from 1 to 1.5 liters a day as an excellent remedy with which to combat intestinal putrefaction.

Comparing then the ethereal sulphates of Period I with those of Period II, there is found a surprising rise in the latter, when the patient was improving rapidly, associated with a decrease or absence of indican.

Whereas they had averaged in Period I about 0.3805 they rose in Period II to 0.4457, an increase of 17 per cent. The ratio of conjugate to preformed sulphates in the first period was 1 to 6.4; in the latter period it rose to 1 to 4.3 in spite of ample daily bowel movements and lavage of the colon.

The amount of nitrogen ingested was smaller and the amount of nitrogen egested was larger in Period I than in Period II.

It is hard to explain how the introduction of large amounts of lactic acid organisms can in any way have contributed to this increase of the ethereal sulphates, since they are supposed, as above cited, to lessen intestinal putrefaction.

The positive nitrogen balance, however, shows that the patient handled with success a larger amount of proteid in her second period, and this may have explained, notwithstanding the decreased nitrogen output, the increase noted.

If the conjugate sulphates be a true criterion of the so-called intestinal putrefaction, we must deduce that, in this case at least, intestinal putrefaction was not a serious etiological factor and the cause of disease must be sought elsewhere than in the putrefaction of proteids. As a matter of fact, the writer has been inclining to the view, to which this lends color, that an important noxious role is played here perhaps by the carbohydrates, particularly the starches. Other clinical evidence indicates much the same, and it can be shown in some of these patients that entire curtailment of proteid other than milk will not help them if they be fed generously with carbohydrates. In fact, as just shown, the proteid intake was actually increased in this present case, before and during the improvement. One case does not warrant postulates on this score, but it is at least suggestive.

It is interesting to note that in the patients who improved a great change appeared in their stools. For example, whereas Case I had had for perhaps forty years from two to five stools daily, of a frothy, loose nature, these became transformed after her new dietary into more mushy, semifformed or formed stools passed but once a day, unless a suppository was resorted to later. We have had the same experience in certain other cases where the carbohydrates were reduced, and there can be but little doubt that these were responsible for the change. There seems to be in this further suggestive association of the carbohydrates with conditions of the disease.

The ammonia in both metabolic periods of Case III was within reasonable limits, though it showed a rise from 3.4 per cent. of the urinary nitrogen in Period I to 5.6 per cent. of the urinary nitrogen

in Period II. This can hardly be interpreted as implying more than would be expected in view of the considerable quantities of lactic acid consumed.

The preformed and total sulphates showed no marked change in the two periods, were of average amount, and interesting chiefly because of their relation to the conjugate sulphates.

We now approach the interesting though difficult question of the fecal bacteria. What role these play in normal physiology is by no means clear, to say nothing of their relation to diseased processes, but increasing investigations point to the desirability of further knowledge along this line, despite the technical difficulties presented. We are well aware of the skepticism with which this field is regarded, and of the fact that until our premises are more firmly established little that is dependable can be expected. It is equally clear, however, that more active effort should be made to utilize what is known, and the present case is an attempt at discovering a clue on which more elaborate work may be based.

It was desirable that bacteriological studies be undertaken in the present connection, but as this is a formidable undertaking, and was impracticable when contemplated, simpler methods were resorted to.

In feeding great numbers of organisms by the mouth, as is done with buttermilk, one would expect that they would reappear in the feces in equal or greater numbers; but this could not be postulated, least of all in the face of clinical improvement. One could not assume that a vast increase in the total number of bacteria within the gut, of whatever kind, could be beneficial or even harmless. It seemed interesting, therefore, to determine if possible what the facts might be in this regard.

Various methods have been advanced for the estimation of the fecal bacteria, but all of them are open to the criticism of inaccuracy.

Strasburger and Schmidt were among the pioneers in this work, but there is grave doubt whether their gravimetric method of centrifugalization or any of its later modifications is of any avail. It has met with disfavor at many hands, though championed by a few, the strongest of whom seem to be MacNeal, Latzer, and Kerr.<sup>4</sup> According to them it is possible by a most painstaking and laborious technique to obtain dependable results, but the present writer was forced by experience to the conclusion that any method which depends upon removal and estimation of the fecal bacteria by centrifugalization is unreliable.

MacNeal and others agree, however, that the method which admits of the nearest approach to accuracy is that of directly counting the organisms. Several modifications of this can be practised, the most available of which seems to be by mixing a

<sup>4</sup> Proc. Soc. Exp. Biol. and Med., New York, 1908-09, vi, 88 to 90.

known quantity of the properly diluted feces with a small amount of citrated normal blood, and, after agitating the whole, counting the ratio of organisms to red cells in a given stained smear. This gives an approximate idea of the number of organisms present, and while having little or no absolute value, is probably dependable in the same hands for relative values of wide variation.

The stools then when passed were at once covered with a solution of 0.5 per cent. HCl and thoroughly mixed to ensure contact of the acid with all parts. They were then sent to the laboratory and worked up as soon as practicable, generally within an hour. More acid of the same strength was added to make a fairly liquid mass, which was then thoroughly rubbed up in a large mortar until of a uniform homogeneous consistency. This was further diluted if necessary, well mixed, then measured, mixed again, and a sample of 5 c.c. taken and diluted to 50 c.c., with the acid solution. A little of this mixture was drawn up in a small capillary tube. An equal amount of a mixture of normal human blood and sodium citrate was then drawn up into the same tube and the two solutions were mixed by blowing in and out on a glass slide. Smears were then made of this, fixed, and stained with Tiedmann's stain (methylene blue and eosin). A definite field of the slide was then chosen and a count made of 500 red blood cells and of the organisms in the same fields. Having used normal human blood with 5,000,000 red blood cells to the cubic millimeter, the proportion follows: 500 is to 5,000,000 as the number of organisms counted is to  $x$ , whence the final calculation is easily made.

By this means the total number of the bacteria of the stools for the first and the second periods were respectively as follows: Period I, 373,750,000,000; Period II, 12,372,000,000,000. This shows a marked increase in the total number in Period II. It was to be expected perhaps, and yet it could not be assumed until proved.

It is to be noted that the stools, in which the bacteria were counted in Period II, were natural or the result of an enema of salt solution, and did not represent colonic washings if they could be kept separate. It was evident before making the final calculation for dilution that in all cases the counts of bacteria were actually higher than in Period I. These counts were made by Dr. Glenn, resident pathologist of the Presbyterian Hospital, to whom the writer desires to express his indebtedness.

The true significance of this finding is not clear, since we know nothing of the types of organisms concerned.

It does seem reasonably apparent, however, that in joint conditions of this kind the mere presence of bacteria in greatly increased numbers within the bowel is not incompatible with improvement, and that these bacteria may play an important role to this end. Since the marked increase in the number of organisms is presumably due to the fermentative or lactic acid type the coincident increase of the ethereal sulphates is hard to explain, and lacking further

data one can merely hypothesize. Further experiments are in progress, with the view of substantiating these observations and determining their significance.

**SUMMARY.** Summing up the general facts indicated by this as yet incomplete study, it is evident that certain joint cases which are rebellious to all other means of treatment, as proved by long trial, can be arrested by means of a proper dietary coupled with colonic lavage.

The dietary can be so greatly modified during the course of improvement as eventually to differ but slightly from that of a normal individual, and the lavage can be quickly dispensed with entirely.

Coincident with the improvement there may occur an increased output of ethereal sulphates and an increased output of fecal bacteria. The former of these is not out of consonance with the view suggested by certain clinical evidence that the carbohydrates are of hitherto unsuspected importance in this connection. The way is opened to more careful study along this line.

There can be no doubt that while the principles on which the above treatment is based are perhaps known to some, they are unfamiliar if not unknown to the vast body of clinicians who attempt the treatment of this omnipresent disease.

Furthermore, there can be no serious question that a definite proportion of these sufferers can be benefited if not cured in this manner, and it is not inconceivable that further study will show most of them to be in this category.

The adoption of these methods should not be attempted except in cases suitably prepared for it or in those free from demonstrably removable cause. These methods should be applied gradually, with due respect for the caloric needs of the individual, and with constant regard for the weight. Only the most painstaking attention to detail will ensure success, and carelessness during or after convalescence will induce relapse.

The careful study, metabolic and otherwise, of cases which improve under this regimen must yield data of real value in deciphering the factors causing joint disease and the means of removing them.

The data here cited seem to form a suggestive beginning.

In conclusion it is a duty and pleasure to express obligation in a number of directions: To the late Dr. John H. Musser, to Dr. S. S. Stryker, Dr. James E. Talley, and Dr. Edward H. Goodman for many courtesies shown in the wards of the hospital; to Dr. Damon B. Pfeiffer, director of the pathological laboratory, for his courteous and obliging coöperation under hampered conditions; to the Board of Managers of the Presbyterian Hospital for the installation of chemical equipment for clinical research; and finally to Dr. Joseph Sailer, through whose interest and coöperation primarily the facilities for the present study were made possible.

## THE HEALING OF GASTRIC AND DUODENAL ULCERS WITH BISMUTH.<sup>1</sup>

BY CHARLES D. AARON, Sc.D., M.D.,

PROFESSOR OF GASTRO-ENTEROLOGY AND ADJUNCT PROFESSOR OF DIETETICS IN THE DETROIT COLLEGE OF MEDICINE; CONSULTING GASTRO-ENTEROLOGIST TO HARPER HOSPITAL, DETROIT.

BISMUTH was used as a medicinal agent as far back as 1786, when Oidier in Geneva recommended it as an infallible remedy for "stomach cramps;" and it has ever since asserted its place in the therapy of gastric affections. As a matter of course, Oidier used bismuth subnitrate (*magisterium bismuti*) quite empirically, without having any knowledge of the pathological anatomy of gastric ulcer or other gastric affections. He found that the bismuth salt had an anodyne effect upon gastric pains, and this discovery was sufficient to ensure its use, regardless of the exact pathology—which, indeed, could not in those days be clearly diagnosticated. About the middle of the nineteenth century Hannon<sup>2</sup> recommended bismuth as an antacid, giving, however, the preference to the subcarbonate. Oppolzer<sup>3</sup> likewise emphasized its antacid effect, and Bricka<sup>4</sup> referred particularly to the astringent effect of the drug upon the gastric mucosa.

It was left for Kussmaul to systematize the therapeutics of bismuth, following certain reflections on the pathological anatomy and physiology involved. His leading train of thought assumed this form: The irritating and painful sensations of gastric ulcer are caused by food remnants settling down at the base of the ulcer, irritating the latter as well as the exposed nerves, and thus causing acid formation and nausea. This can be easily understood as regards old and deep ulcers with elevated margins and incontractible base; and the mere passing of the gastric contents over small and superficial ulcers was held to be sufficient to cause pain. Although these food remnants can be removed by lavage, natural or artificial, this process will not prevent the constant formation of fresh deposits; so the idea suggests itself of providing a covering for the lesion which would protect it from irritation by the passing food. The same requirement follows from a consideration of the healing process. This takes place from the margins, forming granulating tissue toward the base, protecting the ulcer from irritation, and gradually closing the defect. This granulating tissue is very

<sup>1</sup> Read before the annual meeting of the American Gastro-enterological Association at Atlantic City, N. J., June 3 and 4, 1912.

<sup>2</sup> *Presse méd.*, 1856, Nos. 46 to 50.

<sup>3</sup> *Zeitsch. d. K. K. Gesellschaft der Aerzte, Wien*, January, 1857.

<sup>4</sup> Cited after Rodari, *Experimetelles u. Klinisches z. Kenntnis der Beeinflussung der Magensaftsekretion durch Medikamente*, Volkmann's Sammlung klin. Vorträge, 1908, Innere Medizin, Nos. 144 to 146.

vulnerable, especially on the fibrous base of old and large ulcers, so that it falls an easy prey to either mechanical irritation by the ingested food or to the digestive action of the stomach. Therefore, this granulating tissue should be protected if possible—shielded from mechanical or chemical injury, just as a surgeon bandages a granulating wound in order to allow the natural healing process to take its course undisturbed.

Starting from these considerations, Kussmaul laid bismuth under tribute as the best means of securing the desired result. His expectations were realized. In many cases the pathological picture changed with surprising suddenness on the application of bismuth. Patients with old and deep ulcers, who experienced but slight relief from simple irrigations, were suddenly freed from pain; they could partake of food again, enjoyed once more an undisturbed night's rest, recovered their general health in a remarkably short time, and increased in weight. There is no longer a doubt that bismuth has a favorable effect upon the pain and the healing process in gastric and duodenal ulcer. The question now arises, how this favorable effect is to be explained, and whether Kussmaul's premises when introducing the remedy were correct.

The research work on this subject, comprising numerous clinical, anatomical, and experimental studies, has furnished proof of the fact that the protection afforded by bismuth subnitrate in gastric and duodenal ulcer is both physical and chemical.

It has been demonstrated by experiments on dogs, notably those of Matthes,<sup>5</sup> that a few hours after its administration bismuth is evenly distributed over the gastric wall. When the gastric contents were artificially removed, it was found that a protective layer of bismuth similar to a powder bandage had formed on the base of the ulcer. Occasional autopsy findings have shown the same effect in man. From clinical observation, too, it would appear that the bismuth deposit remains undisturbed for days upon the gastric mucosa. Fleiner<sup>6</sup> found that up to two or three days after the introduction of a bismuth suspension, bismuth remnants mixed with mucus could be recovered by lavage. Bismuth, as shown by the x-rays, can remain in the stomach for that length of time. This coincides with the statements of patients in regard to the length of their pain-free periods. After the first introduction of bismuth they are often free from pain during the day and the ensuing night, and sometimes longer.

All these observations have demonstrated the fact that, owing to its physical consistence, its fine distribution, and its high specific gravity, bismuth is capable of forming a layer over the ulcer which mechanically protects it from injury. Possibly, however, this effect

<sup>5</sup> Zentralbl. f. innere Med., 1894, No. 1: Beiträge z. pathol. Anatomie u. allgem. Pathol. 1893, No. 2.

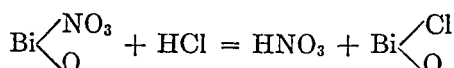
<sup>6</sup> Münch. med. Woch., 1902, No. 23.



is not purely mechanical, but due in part to chemical action. Matthes found that bismuth, when introduced into the stomach, induced a mucous secretion, and that the protective layer was a muco-bismuth mixture. In this process bismuth is reduced to bismuth oxide, and it may be assumed that this is the principal agent in the formation of the bismuth crust.

There is no doubt that bismuth possesses chemical properties, but it cannot yet be definitely stated whether the physical or the chemical property predominates in the relief of pain and the healing of the ulcer. The physical effect is produced by the entire quantity of bismuth introduced, whereas the chemical effect is dependent upon only a small portion of it. Bismuth subnitrate being insoluble in water is chemically inert under ordinary circumstances. A small part of the total quantity introduced in the stomach is decomposed in the acid gastric juice or duodenum, liberating nitric acid, and it is only after this process has taken place that the chemical action of the bismuth begins.

The chemical action of bismuth within the stomach and duodenum is (1) antisecretory, (2) astringent, and (3) antispetic. For the better understanding of these three bismuth effects, it is necessary to appreciate the chemical process which takes place upon the disintegration of the bismuth in the hydrochloric acid gastric contents. The decomposition of bismuth subnitrate takes place according to the following formula:



It has been found that the effective constituent is not the bismuth oxide thus formed, but the simultaneously liberated nitric acid; the three chemical effects above mentioned are due to this factor.

The antisecretory effect of bismuth is best illustrated by an experiment of Rodari<sup>7</sup> upon dogs with a Pawlow fistula (Experiment 15). The experiment may be tabulated as follows:

200 c.c. of water introduced at 7.30 A.M.		200 c.c. of water + 10 gm. bismuth subnitrate (= 5 per cent.) introduced at 1.30 P.M.	
Time.	Quantity of gastric juice.	Time.	Quantity of gastric juice.
8.00 A.M.	3.2 c.c.	2.00 P.M.	2.5 c.c.
8.30 A.M.	2.4 c.c.	2.30 P.M.	0.2 c.c.
9.00 A.M.	2.0 c.c.	3.00 P.M.	0.2 c.c.
9.15 A.M.	1.6 c.c.	3.30 P.M.	0.0 c.c.
9.30 A.M.	0.8 c.c.		
9.45 A.M.	0.0 c.c.		
Period of secretion, 1¾ hours.		Period of secretion, 1½ hours.	
Total quantity of secretion, 10 c.c.		Total quantity of secretion, 2.9 c.c.	
Total acidity, 150.		Total acidity, 120.	

<sup>7</sup> Verhandlungen des Kongresses f. innere Med., 1893.

The other experiments took a similar course.

Rodari distinguishes between the following effects of bismuth subnitrate upon the gastric mucosa:

1. *Healthy Mucosa.* Typical inhibition of secretion, the quantity and probably also the quality of the secretion being reduced. This reaction of a healthy gastric mucosa is the ordinary contingency following the introduction of bismuth subnitrate.

2. *Healing.* Owing to its astringent property, bismuth is capable of producing a direct healing effect. As is well known, astringents precipitate albumin and mucus, entering into combination with the albumin and forming albuminates. This process is particularly favored in the mucous membranes. As a result of the deposition of new, firm particles (the newly formed albuminates) in the tissue interspaces, the epithelial surface is smoothed (condensed) and the size of the bloodvessels diminished. Secretion is, therefore, still further reduced, and the hyperemic conditions and attendant pains are relieved; and the fact that mucous membrane of this consistence is an unfavorable culture ground for bacteria supplies another reason for the subsidence of the inflammatory manifestations. The astringent effect of the bismuth should, however, be only superficial; the result of a deeper action would be tissue destruction or corrosion. The bismuth subnitrate having been decomposed in the acid gastric juice, it is the simultaneously liberated nitric acid which produces the astringent effect. This astringent process is one of the mildest, but may be made to last a long time, since only a small amount of bismuth is decomposed at a time, and the total quantity remains in the stomach for hours together; the dose, however, should be repeated often enough to supply the loss from disintegration. Thus it is possible, with the aid of bismuth, to maintain a uniform gently astringent process for weeks and months.

3. The *antiseptic* effect of bismuth subnitrate, illustrated in surgery by the use of this salt as a dusting powder, is applicable also in gastric and duodenal ulcer—the remedy cleansing the ulcerous base and ensuring a practically antiseptic healing of the ulcer.

The following indications have been gathered from practical experience for the application of bismuth subnitrate in practice:

The first consideration is that it is always desirable to do without any medication whatever in the treatment of gastric ulcer and duodenal ulcer. As a matter of fact, bismuth can never be regarded as a substitute for the rest cure in the treatment of ulcer. Its general purpose is to reinforce this treatment, especially when the latter fails, or when the ulcer takes a chronic course, tends to relapse, or gives rise to considerable pain; and, furthermore, in the treatment of outdoor patients. If in these cases there is hyperacidity, bismuth is so much the more indicated, for it is more effectual in hyperacid cases than in others. Bismuth is least

indicated in cases marked by achylia or subacidity; in the total or comparative absence of hydrochloric acid in the stomach it cannot be decomposed, and its efficiency is restricted to the exercise of its physical properties. From this it follows that bismuth subnitrate is not to be looked upon as a specific for gastric and duodenal ulcer. Its successful application depends principally upon individualization and manner of use. The chief requirement is to have the protective layer over the ulcer large and resistant from the first, and to renew and supplement it at regular intervals. As soon as the subjective complaints are relieved, the daily bismuth dose may be tentatively reduced and, as the treatment proceeds, administered only every second day. If there should be no trouble on the day that bismuth is withheld, the intervals may be extended until finally the treatment is discontinued entirely. In consideration of what has been said about the physical and chemical action of bismuth, it is evident that it should only be administered finely suspended in a liquid medium.

As mentioned before, the practical application of bismuth has extended considerably since Kussmaul's publications on the subject, and has been further generalized and simplified by his pupil Fleiner.<sup>8</sup> At first, Fleiner used the following method of treatment:

The stomach being washed out, as soon as the irrigation fluid returned clear without acid reaction 10 to 20 grams of bismuth subnitrate, well mixed with 150 to 200 c.c. of tepid water, was poured through the funnel. As the tube slowly emptied itself, it was carefully withdrawn, after which the patient was immediately placed in the position corresponding to the seat of the ulcer—in the right decubitus if the ulcer were seated at the pars pylorica, and in the recumbent position if there were reason to believe that the ulcer occupied the lesser curvature.

In order not to inconvenience the stomach too much by the volume of water, Fleiner frequently left the clamped tube in the stomach for a while, until the heavy bismuth had settled, and then, before slowly withdrawing the tube, allowed part of the water to flow off.

According to his present method, the stomach tube is discarded entirely and bismuth suspensions (10 to 20 grams of bismuth subnitrate in a tumbler of warm water) are taken by mouth, in the morning, on an empty stomach, the latter having been cleansed three-quarters of an hour to an hour previously with about 150 c.c. of Carlsbad or Vichy water. The bismuth is given daily, the dose, as before mentioned, being more or less rapidly increased, reduced, or discontinued, according to the clinical course.

The quality of the bismuth preparation used is important. According to Fleiner<sup>9</sup> the best preparation is bismuth subnitrate

<sup>8</sup> Zeitsch. f. klin. Med., 1904, vol. lli.

<sup>9</sup> Loc. cit.

which has been precipitated from a boiling hot mixture, as this is much more finely powdered than a preparation precipitated from tepid or cold fluids.

A modification of this method consists in administering bismuth in oil by combining the bismuth treatment with Cohnheim's oil treatment—which is indeed a very practical and successful method. The doses of bismuth stated above are taken, finely suspended in olive oil, several times daily. According to Stepp,<sup>10</sup> bismuth suspensions in chloroform water are very efficacious:

	Gm. or c.c.
R—Bismuthi subnitratī . . . . .	3
Chloroformi . . . . .	1
Aquæ destillatæ . . . . .	150

M.—Sig.—One to two tablespoonfuls to be taken hourly for several weeks.

It is not unlikely that the chloroform conduces to the anodyne effect. The several methods for the application of bismuth in the treatment of gastric and duodenal ulcer have been fully described by me.<sup>11</sup>

There is no denying the fact that the bismuth treatment is attended with some disadvantages. Liberal and prolonged administration of bismuth is not infrequently followed by constipation, which has to be relieved either by enemas or by a combination of the bismuth with magnesium oxide. It is equally possible that, under certain circumstances, large doses of insoluble bismuth will, in passing through the intestinal tract, cause diarrhea. Nor does every stomach tolerate large quantities of bismuth. In one case bismuth has led to concrement formation in a cavity of the stomach formed by perforation of the ulcer into the pancreas (Fleiner). In a few rare cases intestinal calculi have been formed through the influence of bismuth (Wegele<sup>12</sup>).

There have also been cases in which the bismuth crust became so indurated and was so firmly consolidated with the ulcerous base that the ulcer underneath was prevented from healing, the crust acting like a foreign body. Cases of this kind are not very frequent, but they have occasionally been seen in autopsies and operations. Thus, Naunyn reports the case of a patient who died of gastric hemorrhage, and autopsy showed the gastric ulcer to be covered with a bismuth crust weighing about 20 grams.

A further objection, raised by Elsner, and certainly not without justification, is that the stomach may not have sufficient tonic power to bear a preparation as heavy as bismuth subnitrate administered in large doses and for a long time. Elsner attributes

<sup>10</sup> Berlin. klin. Woch., 1893, p. 983.

<sup>11</sup> Diseases of the Stomach, Lea & Febiger, Philadelphia, 1911, pp. 442 to 446.

<sup>12</sup> Die Therapie der Magen und Darmerkrankungen, Jena, 1905.

the frequently observed constipation to weakness of the intestinal musculature, caused by the heavy bismuth.

All these disturbances, which will occasionally arise, should be considered when deciding upon bismuth treatment. In short, it is necessary to adapt the treatment to the individual case.

Direct failures of the bismuth treatment have been reported by Elsner,<sup>13</sup> Boas,<sup>14</sup> and Zweig.<sup>15</sup> These authors freely acknowledge the anodyne effect of bismuth, but do not think much of its curative effect.

Unfounded reports have been made of poisonous manifestations following the use of bismuth. Fleiner<sup>16</sup> states that, in 1829, Justinus Kerner published the history of a fatal poisoning by subnitrate of bismuth, but later, in 1835, the fact was established that the poisoning resulted not from bismuth, but from hydrargyrum præcipitatum album. It was this erroneous publication of Kerner's that gave bismuth a bad name, from which it has not yet entirely recovered. Other reports on poisoning by bismuth are, in all probability, attributable to the use of impure preparations, containing arsenic and lead. Chemically pure bismuth subnitrate is non-poisonous.

Boas<sup>17</sup> prefers the subcarbonate to the subnitrate, Hannon<sup>18</sup> having previously called attention to bismuth subcarbonate, as mentioned above. The subcarbonate is non-poisonous and probably has the same general effect as the subnitrate, including the antacid effect. An advantage of bismuth subcarbonate is that it colors the feces white, thereby facilitating the recognition of any coarse admixture of blood. Bismuth subnitrate, on the other hand, colors the stool black or greenish black through the formation of bismuth oxide, which may either lead timid patients to erroneously suspect hemorrhage, or conceal an actually existing hemorrhage. An objectionable feature of bismuth subcarbonate is that, on entering into combination with hydrochloric acid of the stomach, it releases a certain amount of carbon dioxide, which under certain circumstances may give rise to considerable distention of the gastric wall and the ulcer. Besides, the beneficial effect of the liberated nitric acid is lost.

Bismuth subgallate is a very acceptable substitute for bismuth subnitrate. It can be freely suspended in water and is non-toxic, but its constipating effect is greater than that of bismuth subnitrate. It can be suspended not only in water, but, as recommended by Ageron,<sup>19</sup> in oil to advantage.

<sup>13</sup> Lehrbuch der Magenkrankheiten f. Aerzte und Studierende, 1909, Berlin.

<sup>14</sup> Diagnostik und Therapie der Magenkrankheiten, 1907, Part II, Leipzig.

<sup>15</sup> Die Therapie der Magen und Darmkrankheiten, Berlin-Wien. 1907.

<sup>16</sup> Loc. cit.

<sup>17</sup> Loc. cit.

<sup>18</sup> Loc. cit.

<sup>19</sup> Münch. med. Woch., 1902, No. 30.

## CONTRIBUTION TO THE BACTERIOLOGY OF PERITONITIS, WITH SPECIAL REFERENCE TO PRIMARY PERITONITIS.<sup>1</sup>

BY MORRIS FISHBEIN, M.D.,

CHICAGO.

(From the Pathological Laboratory of Rush Medical College, Chicago.)

THE purpose of this report is twofold: (1) To discuss the records in the pathological laboratory of Rush Medical College of bacteriological examinations made of material obtained from the peritoneal cavity after death from peritonitis, and (2) to compare the results of this analysis with other similar summarizing reports on the bacteriology of peritonitis.

In a rather thorough search of the literature the only statistical reviews of a similar nature of the bacteriology of peritonitis, as it may be studied by examination of peritoneal fluids made after death, including any considerable number of cases, are those of Flexner<sup>2</sup> and Manahan.<sup>3</sup>

The examinations made in the pathological laboratory of Rush Medical College were undertaken for the most part by students as a part of their routine work and under careful supervision. The postmortem examinations were held in the Cook County Hospital, the Presbyterian Hospital, and in a number of other hospitals in Chicago; a few were in private homes or in undertaking establishments. The report of Flexner includes a summary of the cases observed in the Johns Hopkins Hospital up to 1897 and that of Manahan the records of the Massachusetts General Hospital up to 1905. As the records of the pathological laboratory cover a period of approximately thirteen years previous to 1911, each report overlaps the preceding one by six years.

Anatomically, peritonitis in the records I have studied has been divided into purulent, serofibrinous, fibrinous, acute septic, hemorrhagic, fibrinopurulent, and seropurulent types. Of each form there were: Purulent, 64; serofibrinous, 64; fibrinous, 33; acute septic, 11; hemorrhagic, 6; fibrinopurulent, 6; seropurulent, 2.

The anatomical character of the inflammation does not bear any relationship to the nature of the primary lesion when such exists, nor does it seem to be influenced by the presence of various

<sup>1</sup> Read before the Chicago Pathological Society, April 8, 1912.

<sup>2</sup> Philadelphia Med. Jour., 1898, ii, 1019.

<sup>3</sup> Boston Med. and Surg. Jour., 1905, clii, 346,

bacteria alone or in combinations of various kinds. Various bacteria or the same bacteria cause the same or different forms of peritonitis, and a similar lack of relationship exists between such disease conditions as pneumonia, cholecystitis, appendicitis, salpingitis, etc., in so far as the features of the peritonitis are concerned. In these respects the conclusions arrived at from a study of the records I have examined are confirmatory of those previously made by Flexner and Manahan.

In classifying my records of cases of peritonitis I have used the classification proposed by Flexner in 1898, which seems for all purposes the best possible in that it is simple, distinct, and a real expression of clinical and bacteriological etiology. Previous to that time the classification of Tavel and Lanz<sup>4</sup> proposed in 1893 was the one commonly used. These authors divided all peritonitides into primary and secondary types; the former including blood and lymph infections and being mono-infectious, that is, with one organism, and the latter all other cases, and being polyinfectious. Flexner divided all cases of peritonitis into primary, exogenous, and endogenous types. Primary peritonitis occurs as a result of previous chronic diseases or an infectious focus elsewhere in the body, the infecting organism being brought by the blood or lymph channels to the peritoneum. Exogenous peritonitis occurs as a result of wound infection from gunshot wounds, abortion with sepsis, septic instruments, etc., and includes laparotomies with subsequent peritonitis. Endogenous peritonitis occurs as a result of organisms coming from foci in relation to the peritoneal cavity, the most common cause being various affections of the appendix. Further division is then made into pure and mixed types where one or more than one organism is found.

In the following table, which includes all cases of peritonitis in the Rush records, in which bacteriological examinations were made, is given the classification and number of cases of each type, the organisms found, and their frequency in pure and mixed infections.

<sup>4</sup> Mitteilungen aus klin. u. med. Inst. der Schweiz, 1893.

TABLE I.

Organisms	Primary			Exogenous			Endogenous			Total
	Pure	Mixed	Total	Pure	Mixed	Total	Pure	Mixed	Total	
Colon bacillus . . . . .	3	10	13	1	2	3	27	40	67	83
Streptococci . . . . .	5	7	12	..	2	2	3	18	21	35
Staphylococci . . . . .	3	9	12	1	2	3	4	29	33	48
Pneumococci . . . . .	5	4	9	..	1	1	2	5	7	17
Gas bacillus . . . . .	1	..	1	..	..	..	..	1	1	2
Bacillus proteus . . . . .	..	..	..	..	..	..	1	2	3	3
Bacillus mucosus . . . . .	..	1	1	..	..	..	..	2	2	3
Typhoid bacillus . . . . .	..	..	..	..	..	..	3	3	6	6
Bacillus pyocyaneus . . . . .	..	1	1	..	..	..	1	1	2	3
Bacillus paratyphosus . . . . .	..	..	..	..	..	..	1	..	1	1
Micrococcus tetragenus . . . . .	..	1	1	..	..	..	..	..	..	1
Unidentified . . . . .	..	..	..	..	..	..	2	1	3	3
Sarcinæ . . . . .	..	..	..	..	..	..	..	1	1	1
Bacillus cloacæ . . . . .	..	..	..	..	..	..	..	3	3	3
Combinations:										
Colon bacillus and streptococcus . . . . .	..	2	2	..	..	..	..	6	6	8
Colon bacillus and staphylococcus . . . . .	..	1	1	..	..	..	..	10	10	11
Colon bacillus and pneumococcus . . . . .	..	2	2	..	1	1	..	1	1	4
Colon bacillus and typhoid bacillus . . . . .	..	..	..	..	..	..	..	1	1	1
Colon bacillus and bacillus pyocyaneus . . . . .	..	..	..	..	..	..	..	1	1	1
Colon bacillus and Micrococcus tetragenus . . . . .	..	1	1	..	..	..	..	..	..	1
Colon bacillus and bacillus cloacæ . . . . .	..	..	..	..	..	..	..	2	2	2
Colon bacillus and gas bacillus . . . . .	..	..	..	..	..	..	..	1	1	1
Colon bacillus and bacillus proteus . . . . .	..	..	..	..	..	..	..	2	2	2
Colon bacillus and bacillus mucosus . . . . .	..	1	1	..	..	..	..	1	1	2
Colon bacillus and sarcinæ . . . . .	..	..	..	..	..	..	..	1	1	1
Streptococci and staphylococci . . . . .	..	3	3	..	1	1	..	7	7	11
Streptococci and pneumococci . . . . .	..	1	1	..	..	..	..	..	..	1
Staphylococci and pneumococci . . . . .	..	..	..	..	..	..	..	1	1	1
Staphylococci and typhoid bacilli . . . . .	..	..	..	..	..	..	..	1	1	1
Staphylococci and bacillus pyocyaneus . . . . .	..	..	..	..	..	..	..	1	1	1
Multiple organisms . . . . .	..	3	3	..	1	1	..	8	8	12
Totals . . . . .	17	15	32	2	3	5	44	45	89	125

In the report of Flexner a protocol or short summary of the anatomical diagnosis in each case is given; Manahan classified all



his cases according to various rather well-defined anatomical causes. In the following table I have recorded the significant point in the anatomical diagnosis in each case included in the postmortem records of the pathological laboratory of Rush Medical College, and have followed to some extent the outline of Manahan.

TABLE II.

Sources of peritonitis.	Type.	Cases.
Cause not found or suppurating foci at points distant from peritoneal cavity . . . . .	Primary	18
Salpingitis . . . . .	Endogenous	20
Terminal peritonitis in pneumonia . . . . .	Primary	18
Perforation of small intestine . . . . .	Endogenous	17
Carcinoma of stomach . . . . .	Endogenous	15
Following laparotomy for other than suppurative conditions in peritoneum . . . . .	Exogenous	15
Typhoid ulcer with or without perforation . . . . .	Endogenous	13
Appendiceal abscess . . . . .	Endogenous	11
Extension from adjacent suppuration . . . . .	Endogenous	10
Perforated appendix with abscess . . . . .	Endogenous	9
Carcinoma of genito-urinary tract . . . . .	Endogenous	5
Carcinoma of large intestine or rectum . . . . .	Endogenous	5
Puerperal uterus . . . . .	Endogenous	4
Perforation of large intestine . . . . .	Endogenous	4
Carcinoma of pancreas . . . . .	Endogenous	3
Colotomy . . . . .	Endogenous	3
Extra-uterine pregnancy . . . . .	Endogenous	3
Ulcerative cholecystitis . . . . .	Endogenous	2
Abscess of bladder wall . . . . .	Endogenous	2
Gangrenous pancreatitis . . . . .	Endogenous	2
Ruptured liver abscess . . . . .	Endogenous	1
Perforation of uterus . . . . .	Endogenous	1
Sarcoma or abdomen . . . . .	Endogenous	1
Intestinal obstruction . . . . .	Endogenous	1
Hemorrhagic pancreatitis . . . . .	Endogenous	1
Abortion . . . . .	Endogenous	1
Gastric ulcer, operated . . . . .	Endogenous	1

This includes in all 184 cases, of which there are 39 primary, 16 exogenous, and 129 endogenous. It is at once apparent that there may be considerable overlapping in such a division of sources and some difficulty in determining the classification in one or two cases.

A comparative study of the results included in the three tabulations has been of considerable interest in many respects. It has afforded an insight into the advance of bacteriological study, with facilitation of technique; it has enabled us to arrive more accurately at the true value of various factors involved because of the greater numbers of cases thus brought together, and has enabled us to eliminate any factors determined in the different studies of this nature, which might seem to be related to the various types of material found in special localities. In the following table are included 106 cases summarized by Flexner, 110 cases summarized by Manahan, and 126 cases included in the records I have analyzed in which bacteriological studies were made.

TABLE III.

	Rush.	Flexner.	Manahan.	Totals.
Total number of cases . . . . .	126	106	110	342
Organisms:				
Colon bacillus . . . . .	83	55	45	183
Staphylococcus . . . . .	48	27	8	83
Streptococcus . . . . .	35	54	54	143
Pneumococcus . . . . .	17	8	12	37
Typhoid bacillus . . . . .	6	3	0	9
Bacillus proteus . . . . .	3	6	0	9
Bacillus mucosus . . . . .	3	0	12	15
Bacillus cloacæ . . . . .	3	0	0	3
Gas bacillus . . . . .	2	8	1	11
Bacillus pyocyaneus . . . . .	2	6	0	8
Micrococcus tetragenes . . . . .	2	0	0	2
Bacillus (lactis) aërogenes . . . . .	1	0	0	1
Bacillus paratyphosus . . . . .	1	0	0	1
Unidentified . . . . .	3	8	2	13
Types of infection . . . . .	126	106	110	342
Pure infection . . . . .	63	55	51	169
Mixed infection . . . . .	63	47	37	147
Primary, pure . . . . .	17	9	7	33
Primary, mixed . . . . .	15	1	2	18
Exogenous, pure . . . . .	2	25	10	37
Exogenous, mixed . . . . .	3	9	5	17
Endogenous, pure . . . . .	44	21	34	99
Endogenous, mixed . . . . .	45	37	30	112

"Unreliability of statistics" is an extremely trite phrase. This triteness is in itself an expression of the truth of the statement. Nevertheless, reports of large numbers of cases have in the past resulted in much valuable information, especially in regard to etiology and the results of treatment; they have in many cases indicated prophylaxis. Even after making such full and liberal allowances as can best be made only by one who has labored with such statistics as these, it has seemed to me that some generalization was justifiable.

From the facility and ease with which the cases have been brought under Flexner's classification, it seems proper to point out again that for all purposes such a classification as that proposed by Flexner is to be preferred. It suggests at once both the clinical and bacteriological etiology of the peritonitis, and the route of infection must be of primary importance in the classification of the condition.

The bacteriological results given in Table I were determined by students in the department of pathology of Rush Medical College. During the first half of the thirteen years covered by the records, cultures were made from colonies obtained on plates of plain agar. Since that time the technique has been as follows: Fluids are withdrawn in sterile pipettes and transmitted as soon as possible to the laboratory, where tubes of agar, melted and cooled to 43° C., and mixed with about 8 drops of human defibrinated blood, are inoculated with two dilutions. These are poured into plates and

subcultures are made from colonies developing on these plates. While the results do not indicate by the number and types of organisms found any overwhelming superiority in this latter method, they seem to show that the identification of the organism is made quicker and more often by the latter method. The results included in Flexner's report as well as those of Manahan represent bacteriological studies made by men in all probability better trained in this work. The comparative study of the various results has therefore been of great interest, and seems to show in gross, great similarity.

For the reason that both previous reports included the various combinations in which organisms were found, such a procedure was followed here, although it seems to offer but little in the way of valuable information as to the bacteriological etiology of peritonitis. Occurrence of various organisms in symbiosis is of importance, and in this regard it is worthy of note that both in these records and those reported by Flexner the *Bacillus pyocyaneus* was found together with the colon bacillus, although Dudgeon and Sargent,<sup>5</sup> in a report made in 1905, affirm as a result of numerous experiments, that this is not possible.

The colon bacillus was found 183 times in 342 cases. Its importance as a factor in the bacteriology of peritonitis will at once be conceded, but the point of interest is as to whether it occurs singly in any large proportion of cases or is usually associated with some other organism. Flexner found 11 single infections and 44 multiple, Manahan found 12 single and 33 multiple, and I have found 31 pure and 52 multiple. We must therefore conclude that the colon bacillus most commonly occurs mixed with other organisms and that it may quite often occur singly. Further analysis shows that it is seldom if ever a blood infection, and that in all cases of primary peritonitis where the colon bacillus is found it is probably the second invader.

The staphylococci, according to the records of the Rush Pathological Laboratory, occur more commonly than would seem to be the case from the reports of Flexner and Manahan. It is generally known that the staphylococcus may often be a contaminating organism in amateurish bacteriological work. However, in the report of Dudgeon and Sargent, which includes records of bacteriological examinations of peritoneal fluids taken at the time of operation, the staphylococcus was found in 108 of 270 cases. This seems to be the only report of this character in the accessible literature, and it would seem to indicate that a large proportion of staphylococci in peritoneal fluids is to be expected rather than not.

As a virulent organism commonly associated with septicemia, the importance of the streptococcus as a causative factor in peritonitis, especially the primary type, is at once apparent. Its occurrence

<sup>5</sup> Lancet, 1905, i, 473.

in cases of peritonitis where a septicemia is present is shown by Manahan, who found septicemia present in 32 of 110 cases, the streptococcus being present in 24, pneumococcus in 5, and the staphylococcus in 2. From the cases included in Table I it was found that the pneumococcus was of more importance than the streptococcus as regards the association of peritonitis with a septicemia.

In none of the reports was record made of the presence of the gonococcus in peritoneal fluids examined post mortem.

The relative importance of the pneumococcus in recent years is well expressed by the numerical ratio shown by the records of Flexner, Manahan, and the Rush records respectively. It seems to be particularly associated with primary peritonitis, and the literature of the last few years contains many reports of primary pneumococcic peritonitis.

The typhoid bacillus occurs in peritoneal fluid in cases of peritonitis where there is a perforation of the small bowel or where no such perforation exists. All these cases have been classified as endogenous, although, as is obvious, some may have been primary, or all, in which no perforation was found, may have been primary.

Bacillus mucosus is of importance as shown by the figures given, and the gas bacillus is a common finding in all cases of feculent peritonitis.

The majority of all cases of peritonitis are endogenous in character and are due to a combination of the colon bacillus and other organisms, usually staphylococci and streptococci.

Exogenous peritonitis occurs much less commonly with perfecting of operative aseptic technique and with lessening of exploratory laparotomy, instrumental abortion, etc.

The records of the Rush Laboratory include 39 cases of primary peritonitis in 184 cases, or 25 per cent., as contrasted with 10 per cent. in the reports of Flexner and Manahan. Primary peritonitis, which includes blood and lymph infections, both from infected foci elsewhere in the body or from previous chronic disease, or all cases apparently idiopathic, forms a larger proportion of acute cases than is commonly supposed. For this reason and because of the interest attached to this subject a further analysis was made of all cases coming under this classification and a rather thorough search of the astonishingly meagre recent literature was undertaken with a view to summing up the reports to the present time.

**PRIMARY PERITONITIS.** In the decade from 1870 to 1880 the subject of idiopathic peritonitis received considerable attention from various writers (Collie,<sup>6</sup> Lewis,<sup>7</sup> Meade,<sup>8</sup> Semple<sup>9</sup> and others), who advanced various theories as to its origin without any actual basis upon which to found their conclusions. They considered the

<sup>6</sup> Med. Exam., London, 1877, ii, 843.

<sup>8</sup> British Med. Jour., 1876, ii, p. 393.

<sup>7</sup> Trans. Med. Soc. New York, 1873, p. 143.

<sup>9</sup> Med. Exam., London, 1878, iii, 553.

subject from a purely clinical standpoint, and attempted to solve the origin of the condition, finally associating it with sleeping in a draught, catching cold, etc.

Flexner, in 1897, called attention to the classification of Tavel and Lanz, previously mentioned, and the relation of the apparently idiopathic peritonitis to blood and lymph infections, when a previous chronic disease occurred in an individual, or where there was an infectious focus elsewhere in the body.

Nothnagel,<sup>10</sup> in 1901, argued against such an hypothesis, but stated "that the last word on this subject must come from the pathologist, not the clinician." He states that in 13 cases reported by Grawitz from a total of 867 none would bear close criticism. To him it was clear that although theoretically any causes acting on the pericardium, pleura, or meninges to set up inflammation might act as well upon the peritoneum, careful scrutiny would reveal in all supposedly primary cases some endogenous source for infection. He mentioned a case in which a patient caught cold, the tonsils being found much infected with a form of streptococcus. In a subsequent supposedly primary peritonitis the same type of organism was found. The explanation advanced by Nothnagel is that the patient swallowed mucus containing these streptococci, and that they gained their entrance to the peritoneum through the stomach wall rather than by a blood or lymph infection. In view of the results of modern investigation with recovery of organisms from the blood in similar cases these suggestions of Nothnagel become of interest only in a historical way.

Armstrong<sup>11</sup> in 1903 found 5 cases of primary peritonitis in 102 autopsies. Osler in an analysis of 102 autopsies from earlier records found 12 cases. "In every instance," says Armstrong, "the subject was a female." In 2 instances the streptococcus was found, in 1 the pneumococcus, and in 2 no bacteriological studies were made. The fact that all these cases occurred in females seems to suggest to Armstrong that the uterus and Fallopian tubes were the mode of entrance of the organisms. In other words, they would be exogenous rather than primary. He also suggested that a *locus minoris resistentia* in the peritoneum may be established by shutting off the blood supply, not uncommonly by caseating tuberculous retroperitoneal lymph glands, and bacteria brought by the blood, or through the pleura or tubes set up an infection.

The opinion of Spencer<sup>12</sup> in a report in which he discusses several cases of apparently idiopathic peritonitis is that in every instance the bacteria must come from the intestines or stomach or other organs within the abdominal cavity. He does not consider the blood or lymph routes of infection as possibilities.

<sup>10</sup> Wien. med. Presse, 1901, xlii, 1321.

<sup>11</sup> Montreal Med. Jour., 1903, xxxii, 728.

<sup>12</sup> Westminster Hosp. Rep., London, 1907, xv, 18.

In a report of several cases by Sheldon<sup>13</sup> in 1902 the work of Hawkins, who showed that an appendix may appear perfectly normal and still contain minute abscesses which give rise to infection, is supported. Sheldon concludes that in all cases of apparently idiopathic peritonitis, organisms gain access to the peritoneum from the intestines or other organs within the abdominal cavity.

Of the 39 cases of primary peritonitis in 184 cases included in the Rush records in 18 instances a pneumonia was present. In order to make clear the conditions existing in the other cases a short abstract of the chief points in the anatomical diagnosis of each case is given.

CASE I, No. 630.—Acute serofibrinous peritonitis. *Micrococcus tetragenes*; colon bacillus. Cardiac hypertrophy; emphysema and purulent bronchitis; acute and chronic pleuritis and empyema; cirrhosis of the liver, with gummas; cholelithiasis; chronic gastric catarrh.

CASE II, No. 732.—Acute serofibrinous peritonitis. *Bacillus pyocyaneus*; colon bacillus. Chronic tuberculous cavities in the lungs; chronic disseminated pulmonary tuberculosis; marasmus.

CASE III, No. 859.—Acute serofibrinous peritonitis. No bacteriological study made. Premature birth; congenital syphilis; double white pneumonia; osteochondritis.

CASE IV, No. 938.—Diffuse fibrinopurulent peritonitis. *Micrococcus tetragenes*; colon bacillus; *Streptococcus pyogenes*. Hyperplasia of lymphoid tissue in intestinal canal; emphysema and atelectasis of lungs; cloudy swelling of liver and of kidneys; acute splenitis; hypertrophy of left ventricle; hypoplasia of aorta; tonsils enlarged, dark red, and soft on section.

CASE V, No. 959.—Fibrinous peritonitis. No bacteriological study made. Enlarged retroperitoneal and mediastinal lymph glands; right fibrinous pleuritis; edema of lungs; interstitial myocarditis; chronic inflammation of the gall-bladder; hypertrophy of tonsils.

CASE VI, No. 966. Diffuse fibrinopurulent peritonitis. *Staphylococcus albus*. Vaccination wound of right leg; suppurative adenitis of right deep inguinal and iliac glands; purulent infiltration of retrocecal tissue.

CASE VII, No. 996.—Fibrinous peritonitis. Gas bacillus. Puerperal uterus; general invasion of gas-producing organisms.

CASE VIII, No. 1059.—Serofibrinous peritonitis. No bacteriological study. Small white kidney; acute bronchitis, with abscess formation in adjoining lung tissue.

CASE IX, No. 1133.—Fibrinopurulent peritonitis. *Staphylococci*. Fibrous and fibrinous pleuritis; acute vegetative aortic endocar-

<sup>13</sup> Med. Record, 1902, lxii.

ditis; acute splenitis; puerperal uterus; hyperplasia of lymphoid tissues in intestines.

CASE X, No. 1262.—Purulent peritonitis. Colon bacillus. Multilobular fatty atrophic cirrhosis of liver; icterus; ascites; arteriosclerosis (slight); dilatation of esophageal and hemorrhoidal veins.

CASE XI, No. 1312.—Fibrinous peritonitis. Streptococcus. Acute aortic endocarditis; organizing fibrinous pericarditis; cardiac dilatation and hypertrophy; fibrinous pleuritis.

CASE XII, No. 1349.—Fibrinopurulent peritonitis. Pneumococcus; colon bacillus. Fatty degeneration of heart and kidneys; goitre.

CASE XIII, No. 1613.—Serofibrinous peritonitis. No bacteriological study made. Atrophic cirrhosis of liver; dilatation of esophageal veins; chronic endocarditis.

CASE XIV, No. 1645.—Fibrinous peritonitis. Staphylococci. Atrophic cirrhosis of liver; ascites; general anasarca; icterus; chronic valvular and mural endocarditis; chronic pleuritis; postmortem fat necrosis in pancreas.

CASE XV, No. 1636.<sup>14</sup>—Serofibrinous peritonitis. Colon bacillus; staphylococcus. Generalized blastomycosis.

CASE XVI, No. 1692.—Serofibrinous peritonitis. Pneumococcus. Seropurulent arthritis of knee-joint; acute mediastinitis; acute hyperplastic splenitis; hyperplasia of intestinal lymphoid tissue.

CASE XVII, No. 1701.—Fibrinous peritonitis. Colon bacillus; streptococci. Diabetes; gangrene of toe; acute nephritis; tuberculosis of sacro-iliac synchondrosis; chronic mural endocarditis; suppurative sternoclavicular synovitis; psoas abscess.

CASE XVIII, No. 1734.—Serofibrinous peritonitis. No bacteriological study made. Atheromatous ulcers of aorta, with multiple thrombi; embolism of superior mesenteric artery; infarction of small intestines; multiple foci of necrosis in pancreas.

CASE XIX, No. 1768.—Serofibrinous peritonitis. Streptococcus. Acute hyperplastic tonsillitis. Hyperplasia of all lymph glands; small localized abscess in right lower lobe of lung; edema of larynx.

CASE XX, No. 1802.—Fibrinous peritonitis. Colon bacillus; streptococcus. Puerperal uterus; septic endometritis, suppurating corpus luteum of pregnancy.

CASE XXI, No. 1808.—Serofibrinous peritonitis. Streptococcus. Chronic parenchymatous nephritis; pleuritis; chronic pericarditis; cystitis; gastritis.

In 18 cases, as already stated, pneumonia existed, with large numbers of pneumococci in the lung and circulation. In 7 cases there was an associated endocarditis, chronic in type, and often also pleuritis. In 4 cases hyperplasia of lymphoid tissue was marked.

<sup>14</sup> E. E. Irons and E. A. Graham, Jour. Infect. Dis., 1906, iii, 666.

In 4 cases suppurative foci were present elsewhere in the body, distant from the peritoneum. Besides these, there was 1 case of marasmus in tuberculosis, 1 case of premature birth with congenital syphilis, and a case of generalized blastomycosis. In 3 cases a cirrhosis of the liver was present.

A tonsillar lesion is believed often to form the point of entrance for organisms which bring about an endocarditis or pleuritis, and grouping together the cases in which there were endocarditis and hyperplasia of the lymphoid tissue in the throat we find that the streptococcus was found four times, the staphylococcus twice, and in 2 cases no bacteriological studies were made. In the 12 cases of primary peritonitis reported by Flexner the streptococcus was found five times and the staphylococcus twice. The inference that some relationship exists is fully justifiable, and after pneumonia such a condition as this might well be looked for in all cases of supposedly primary idiopathic peritonitis.

The case of terminal peritonitis in congenital syphilis in an infant is of interest because of the not uncommon occurrence of such peritonitis as the causal factor of death in infants whose resistance is lowered. Thus Holt<sup>15</sup> reports a fibrinopurulent peritonitis of unknown origin in a male child, aged six months, in whom the streptococcus was isolated from the peritoneal fluid, and mentions 6 other cases in his own experience. Dr. H. F. Helmholtz<sup>16</sup> has described to me 3 cases which he examined thoroughly and in which he could find no demonstrable source for infection. In such instances it might well be that bacteria had passed from the throat to the blood and thence to the peritoneal cavity.

**SUMMARY.** Peritonitis would seem therefore in the light of the results here given to be most commonly associated bacteriologically with a combination of the *Bacillus coli* and other organisms, usually staphylococci and streptococci. The origin clinically is usually endogenous, affections of the appendix being of major importance, the female organs of generation being next in importance. Exogenous peritonitis is becoming exceedingly rare with improvement of aseptic technique in the handling of wounds and in operative methods.

As has been mentioned, but one complete report of bacteriological conditions in peritonitis at the time of operation is available. The work of Dudgeon and Sargent gives conclusions somewhat at variance with those determined by postmortem examinations of peritoneal exudates, and should therefore be confirmed, with a view to arriving at the relation between the condition existing at the time of operation and that found post mortem. In connection with this point it is of extreme interest to note that

<sup>15</sup> Arch. Pediatrics, 1906, xxiii, 278.

<sup>16</sup> Personal communication.



recently the question of the relation of anaërobic bacteria to appendicitis particularly is attracting much attention. Runeberg<sup>17</sup> and Heyde<sup>18</sup> have shown that in many instances of appendicitis anaërobic predominated over aërobic bacteria and agglutinated with the patient's serum in higher dilutions. Other writers, basing their conclusions upon similar experiments, state that *Bacillus coli* is of most importance etiologically (Kotzenberg<sup>19</sup> and Klienberger<sup>20</sup>). It would seem therefore that both aërobic and anaërobic cultures and determinations had best be made in all instances.

The gonococcus has never been demonstrated culturally in peritoneal fluids post mortem according to the various reports of large numbers of cases. By the clinical history in many instances we are led to believe that the gonococcus is the exciting cause of many peritonitides. In all probability, therefore, its presence has not been shown because of lack of development in cultivating methods or because no special efforts have been made to secure it. Because of its great clinical importance this fact should not be overlooked in future work of this nature.

Primary peritonitis is more common than is ordinarily supposed. In this report 25 per cent. of all cases are of the primary type. Each of these cases is a subject for investigation. In practically all cases there is a lowered resistance of the individual due to some chronic condition, as atrophic cirrhosis of the liver, chronic endocarditis and tonsillitis, marasmus, diabetes, etc. In such conditions the resistance of the peritoneum must be lowered to such an extent that where ordinarily the highly resistant tissue might combat infection with organisms carried by the blood stream, in such instances it becomes the seat of an acute peritonitis which may prove fatal unless proper handling be undertaken after the condition is recognized. In other conditions where a suppurative focus exists elsewhere in the body, or where an infected puerperal uterus, or acutely infected tonsils pour virulent bacteria into the blood stream, we have the other factor for a terminal or acute infection of the peritoneum—namely, a virulent organism. In still other cases, where we have both virulent organisms in large quantity and a lowered resistance of the individual, we may readily have a condition resembling an endogenous peritonitis, where through rupture of an appendix, for example, large quantities of bacteria and toxic material are poured out upon an intact peritoneum, the latter lowering its resistance and the former setting up an acute peritonitis. It would seem then that the word "idiopathic" could be entirely dispensed with in regard to peritonitis, as mani-

<sup>17</sup> Studien über die bei peritoneal Infectionen appendik. Ursprungs vorkommenden Sauerstofftoleranten sowie oblig. anaerob. Bakterien formen. Arb. a. d. path. Inst. d. Univ. Hel-singfors. Berlin, i, 271, 1908.

<sup>18</sup> Beitr. zur klin. Chir., 1911. lxxvii, 1.

<sup>19</sup> Deut. med. Woch., 1909, xxxv, 201.

<sup>20</sup> Deut. Arch. f. klin. Med., 1907, xc, 267.

manifestly close scrutiny yields some source for the condition. The bacteria gain entrance to the peritoneal cavity and the inflammation of the peritoneum is a manifestation of their presence. In the absence of a known exogenous or a demonstrated endogenous source it is important to determine whether any means by which the organisms gained entrance into the blood or lymph stream is demonstrable.

## THE PROGNOSTIC SIGNIFICANCE OF THE ATROPINE REACTION IN CARDIAC DISEASE.<sup>1</sup>

BY JAMES E. TALLEY, M.D.,

VISITING PHYSICIAN TO THE PRESBYTERIAN HOSPITAL, PHILADELPHIA.

My interest in the influence of the vagus on the rate of the heart beat was awakened last year while working in Dr. James Mackenzie's wards in the Mt. Vernon Hospital, London. For the many courtesies shown me by Dr. Mackenzie, Prof. Cushny, Dr. Marris, and other co-workers in the clinic I am deeply grateful. The work on which this paper is based was done largely during my term of service last year in the Presbyterian Hospital, Philadelphia. I appreciate the kindness of my colleagues of the medical staff who placed material at my disposal. It is regrettable that suitable material and the necessary leisure to use it so often fail to come together in point of time.

The recapitulation of a few facts concerning the normal physiological influence of the vagus on the rate of the heart beat may not be out of place. Stimulation of one or both vagi by a rapidly interrupted induction current slows or stops the heart. Such vagal stimulation lessens the conductivity, but does not destroy the irritability of the heart, since direct strong mechanical stimuli may provoke a beat even during cardiac standstill due to vagal stimulation. Conversely, section of one vagus produces some acceleration of the pulse; section of both vagi causes greater acceleration. These phenomena are constant in the vertebrates and prove that the vagi are the normal paths by which travel continually restraining impulses from the inhibitory centres in the medulla to the heart. Physiologists have also found it a constant experience that atropine produces a decided increase in the cardiac rate by paralysis of the vagi. Clinicians find that a hypodermic injection of grain  $\frac{1}{50}$  to grain  $\frac{1}{25}$  of atropine produces the same effect. Physiologists have further shown that atropine acts on the vagi, and not on the muscular substance of the heart, by the observation

<sup>1</sup> Read before the College of Physicians of Philadelphia, March 6, 1912.

that in early embryos, so young that no nerves have yet grown to the heart, the drug has little or no effect.<sup>2</sup>

After making dozens of injections of atropine, grain  $\frac{1}{25}$  in robust males, and grain  $\frac{1}{50}$  in females and less robust males, the writer has yet to see any untoward effect, or hear any decided complaint. The patient should be told that the throat will become dry, and ability to read may be lost for part of the day. Almost always the patient is ready for the next meal, rarely complains of insomnia, and the following day reads as usual. The same has been true in those cases of rebellious hemoptysis where the same doses of atropine have been used.

Professor Cushny suggested the releasing of the vagus by means of hypodermic doses of atropine, so-called atropine reaction, in the study of digitalis action. Silberberg<sup>3</sup> made use of it in studying the action of digitalis in cardiac disease, especially auricular fibrillation. His paper will be referred to later. The method of taking the reaction is thus: The recumbent patient is made as comfortable as possible, the arm supported on a pillow or folded sheet, the ink polygraph applied to the right radial, the engine started at slow speed, and the pulse rate taken graphically for about ten minutes, so as to obtain an average pulse rate before atropine. Throughout the minutes are marked off by touching the time marker every minute by the watch. This makes a slight break in the line, which simplifies the counting later. The hypodermic of atropine is now given in the other arm, while the engine is still running, and the pulse rate taken continuously for another fifty to sixty minutes. The influence of the drug, ordinarily dry throat, may appear as early as twelve to fifteen minutes, but on the average in twenty minutes. The maximum is usually reached in from twenty to thirty minutes from the time of injection, and usually there is no further rise after this or at least after the hour. Just how long the influence may last I have not had time to determine, but in a few cases, when taken at three to five minute intervals, during the second hour there has been no further rise. Counting the pulse rate from the long rolls of paper and setting them down in order in a column shows at a glance when the maximum is reached. The graphic representation by means of loci curves (Fig. 1) shows the contrasts better. The pulse rate before atropine is the average for the ten minutes before the hypodermic. The reaction or the pulse rate after the atropine is determined in this paper by taking the average for ten minutes when the pulse rate is at its maximum after the injection.

The writer started out with two ideas: One was to determine the atropine reaction in hearts as normal as the material available

<sup>2</sup> Halliburton, Handbook of Physiology, p. 256.

<sup>3</sup> Proc. Royal Soc. Med., iv, 192 (1910-1911).

furnished. Of course, the medical wards of a hospital are not ideal places to look for absolutely normal hearts, yet many are approxi-

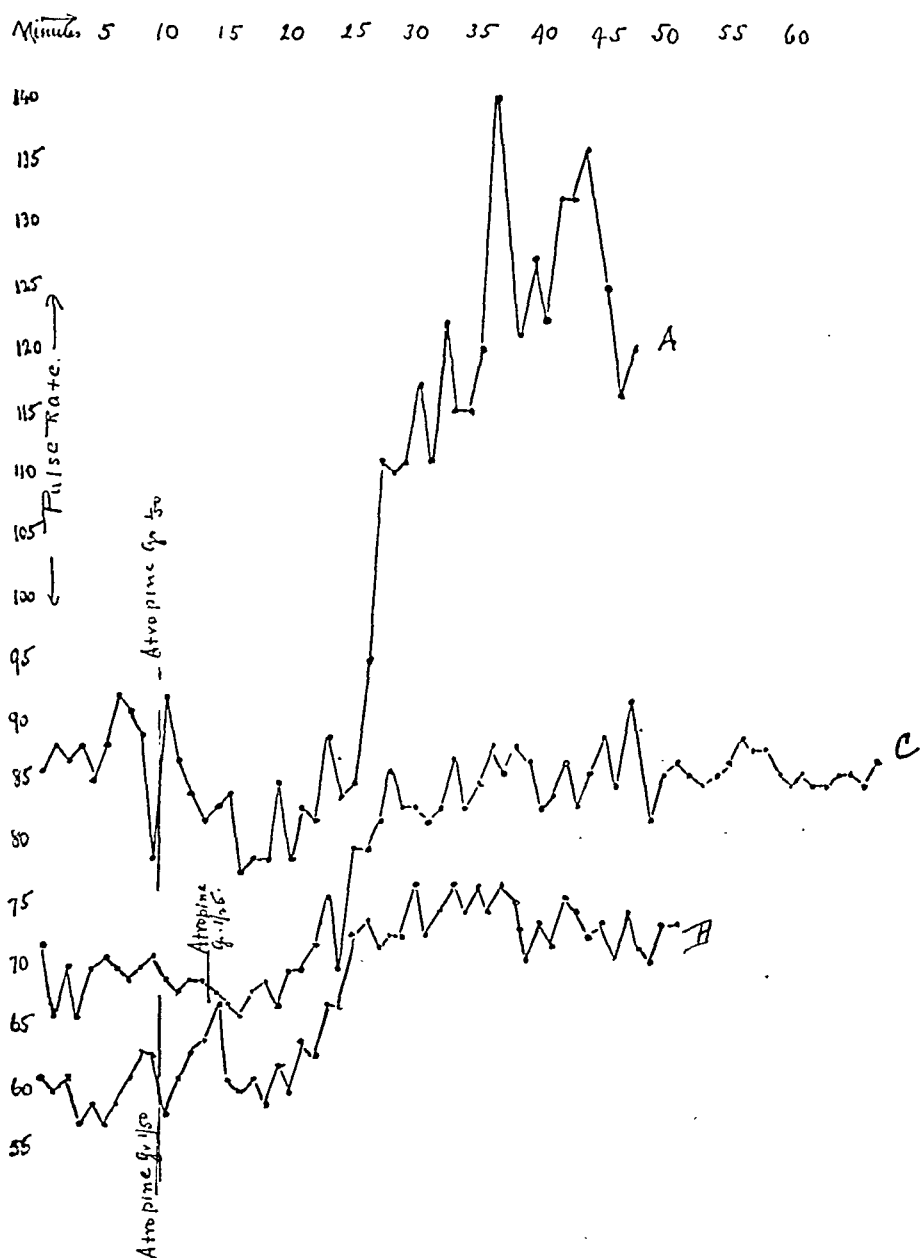


FIG. 1.—Curve A represents the influence of atropine, grain  $\frac{1}{50}$ , in Case I, Table II, before digitalis. Curve B represents the influence of atropine, grain  $\frac{1}{50}$ , in Case I, Table II, on full digitalis. Curve C represents the influence of atropine, grain  $\frac{1}{50}$ , in Case No. 14, Table I.

mately so. The individual outside with a perfect cardiovascular apparatus is not keen to lend himself to such determinations, because it may mean loss of time if the atropine happens to paralyze

accommodation. Having obtained four reactions in persons with approximately normal hearts, there was no difficulty in obtaining plenty of contrasting material, as will be shown by Table I. The other idea was to use the reaction in the study and treatment of patients with cardiac disease. Unfortunately too many of the available cases were of the regular pulse type. However, several studies will be embodied in Table II.

TABLE I.—The patients in Table I, except the last four, had at least no gross lesions of the heart. Nos. 1 and 4 were apparently entirely normal, and Nos. 2 and 3 were so far from their original attacks as to be practically so. They were having extension or superheated air for the old lesions in the joints. Taking these 4, though inadequate, I know, for a working basis, we may look upon the normal reaction as from 30 to 40. The actual average of the 4 is 34. The next ten observations were made in patients who had grossly normal hearts, however these hearts had all been subjected to a chemical poison (No. 5), or the toxins and fever of enteric (Nos. 6 to 10). As the pulse rate, the vagal influence being withdrawn, depends upon the inherent activity of the rhythm giving portion of the heart, it was expected there might be a difference in reaction, and, broadly speaking, this was found true. The exhausted cardiac tissue showed a lessened rather than an increased irritability. Observation 5a was clear when the fault in technique was discovered. In 5b the small reaction is probably due rather to the toxic material in the circulation, due to the acute kidney irritation, than to any influence of the possibly absorbed bichloride of mercury itself on the heart muscle. This view is supported by the normal reaction obtained in observation 5c, the kidneys having cleared up in the two weeks intervening. All the enteric cases (Nos. 6 to 10) give a reaction that is less than normal. In cases Nos. 6 and 7, though a week intervened between the two reactions in each case (6a and 6b, and 7a and 7b), the second reaction was less than the first in each case (6a, 24; 6b, 18; 7a, 24; 7b, 17). One would have expected that after a week, the heart having recovered somewhat, the reaction would have been greater rather than less. The same thing is evident in taking the whole group. The longer a patient has had a normal temperature, the higher the reaction does not follow. For example, Case 10, with temperature normal thirty days, gives a reaction of 12, while 6a and 7a, with normal temperature for seven and nine days respectively, give each a reaction of 24. The small reaction of these enteric cases reminds one of the similar reaction in the senile cardiosclerosis cases. Here the morbid processes leading to slight response are probably but temporary, while the degenerative process in the cardiosclerosis cases are permanent.

TABLE I.

No.	Sex.	Age.	Diagnosis.	Blood Pressure.	Date.	Pulse rate before atropine.	Pulse rate after atropine.	Full vagal effect.	Dose of atropine.	Throat dry. Minutes.	Remarks.
1	F.	18	Hysteria	110-80	October 10	102	132	30	1/25	20	Patient well.
2	F.	21	Old gonorrheal arthritis (hand)	120-60	September 21	95	121	26	1/50	23	No fever for one month.
3	M.	25	Old gonorrheal arthritis (knee)	111-65	October 20	71	111	40	1/25	30	Acute attack months before.
4	F.	48	Gastropoiosis	145-75	November 20	89	129	40	1/50	18	Patient admitted for operation.
5a	M.	24	Acute corrosive sublimate poisoning	130-75	September 27	73	68		1/25		Tablet undissolved in syringe.
5b	M.	24	Acute corrosive sublimate poisoning	134-60	September 28	77	93	16	1/33	20	Urine full of albumin and casts.
5c	M.	24	Acute corrosive sublimate poisoning	110-60	October 11	61	101	40	1/25	18	Urine practically normal.
6a	M.	35	Enteric fever	120-70	October 6	66	90	24	1/25	25	Seventh day of normal temperature.
6b	M.	35	Enteric fever	100-55	October 14	100	118	18	1/25	15	Fifteenth day of normal temperature.
7a	F.	34	Enteric fever	100-55	November 29	104	128	24	1/50	20	Patient up and around.
7b	F.	34	Enteric fever	..	December 6	114	131	17	1/50	17	Ninth day of normal temperature.
8	M.	29	Enteric fever	125-60	October 17	89	109	20	1/25	24	Sixteenth day of normal temperature.
9	M.	21	Enteric fever	120-57	October 2	113	120	7	1/25	20	Patient up and around.
10	F.	18	Enteric fever	..	September 30	99	111	12	1/50	18	Tenth day of normal temperature.
11	F.	29	Small tumor pressing on right vagus	..	June 21	66	130	64	1/50	19	Fourteenth day of normal temperature.
12	M.	45	Mitral disease; auricular fibrillation	125	August 11	101	115	14	1/25	20	Patient up and around.
13	F.	26	Mitral disease; auricular fibrillation	..	July 28	109	143	34	1/50	20	Bradycardia; extrasystoles.
14	M.	60	Cardiosclerosis	170	August 19	70	87	17	1/25	16	Thirtieth day of normal temperature.
15	F.	22	Mitral and aortic disease	108-90	September 29	68	99	31	1/50	25	Patient up and around. Extrasystoles; auricular and ventricular; P-R normal. Pulse always regular; venous pulse, auricular type.

TABLE II.

No.	Observation.	Sex.	Age.	Diagnosis.	Blood pressure.	Date.	Pulse rate before atropine.	Pulse rate after atropine.	Full vagal effect.	Vagal factor in digitalis.	Tissue factor in digitalis.	Dose of atropine.	Amount of digitalis taken.	Throat dry. Minutes.	Remarks.
Ia	Before digitalis	M.	35	Mitral stenosis; auricular fibrillation	..	June 7	90	130	40	..	..	1/50	..	27	Two doses, grain 1/50, atropine; second half-hour after first.
Ib	Full digitalis	M.	35	Mitral stenosis; auricular fibrillation	..	June 21	61	75	..	29	14	1/50	514	18	
Ic	Before digitalis	M.	35	Mitral stenosis; auricular fibrillation	..	July 3	95	145	50	..	..	1/25	..	45	
Id	Full digitalis	M.	35	Mitral stenosis; auricular fibrillation	..	July 26	63	75	..	32	12	1/50	514	26	Two to one heart block.
IIa	Before digitalis	F.	20	Mitral disease; auricular fibrillation	..	June 15	112	148	36	..	..	1/25	..	20	
IIb	Full digitalis	F.	20	Mitral disease; auricular fibrillation	..	July 3	55	56	..	57	1	1/25	514	15	
IIIa	Before digitalis	M.	45	Mitral disease; auricular fibrillation	110—75	May 28	87	115	28	..	..	1/25	..	30	
IIIb	Full digitalis	M.	45	Mitral disease; auricular fibrillation	115—65	July 5	51	80	..	36	29	1/25	534	30	
IIIc	On digitalis	M.	45	Mitral disease; auricular fibrillation	85—55	June 13	85	117	..	2	32	1/25	59	24	
IVa	Before digitalis	M.	35	Cardiosclerosis; auricular fibrillation	145	July 28	60	78	18	..	..	1/50	..	25	Phases of partial block and tachycardia before digitalis.
IVb	Full digitalis	M.	35	Cardiosclerosis; auricular fibrillation	..	August 31	60	60	..	0	0	1/50	532	24	
Va	Before digitalis	M.	71	Cardiosclerosis; heart block	132—65	December 17	77	96	19	..	..	1/50	..	20	
Vb	Full digitalis	M.	71	Cardiosclerosis; heart block	172—102	January 1	42	106	..	35	64	1/33	.. <sup>1</sup>	20	Six days after crisis.
Vc	On digitalis	M.	71	Cardiosclerosis; heart block	..	December 23	80	82	..	..	2	1/50	.. <sup>2</sup>	20	
VIa	Before digitalis	M.	14	Heart sound; after pneumonia	95—45	December 23	73	103	30	..	..	1/50	..	25	
VIb	On digitalis	M.	14	Heart sound; after pneumonia	102—50	January 6	74	114	..	0	40	1/50	57	24	

Infusion 15 ounces; digitalone, 5v.

<sup>2</sup> Infusion 7 ounces.

Case 11 was a patient of Dr. W. E. Robertson's, with whom I took her atropine reaction. She had a small tumor either involving, or at least pressing upon, the right vagus, which gives her a bradycardia. Her pulse during the day we took the reaction had been 36. The emotional disturbance of having a new procedure tried was probably responsible for the average rate of 66 before the atropine. The reaction of 64 reminds one of the response often given by cases of auricular fibrillation with a high pulse rate before atropine. In such cases the bundle is supposed to be in a highly irritable condition, and to carry too many impulses from the disorderly auricle. That her heart was irritable is shown by the great number of extrasystoles in the tracing even during the time she was under the influence of atropine. Atropine more often abolishes the extrasystoles. Dr. Robertson will report the case in full probably after operation. The remaining cases (Nos. 12 to 15), though they are patients with definite cardiac lesions, are included more naturally in Table I, as they were not taken after full digitalis also. They will be referred to later.

TABLE II.—The capital paper of Silberberg has already been mentioned. He shows the prognostic significance of the atropine reaction in cardiac cases especially auricular fibrillation, and how it may be used in the study of digitalis action. My cases add nothing new, but are simply fresh illustrations of some of the facts set forth by him. Now let us compare the atropine reaction in some of these fibrillation cases before they are given any digitalis, or any treatment except rest in bed. First of all cases of cardio-sclerosis, both those with regular pulse and those developing auricular fibrillation, especially if they have a slow rate, most often give a small reaction to atropine. There are exceptions. Table II, IVa, reaction 18, and Va, reaction 19, are illustrations of the first statement. Table I, No. 12, though his initial pulse was 101 gave a reaction of only 14. Table I, No. 14, whose sclerosis was unmistakable, with no fibrillation, gave the same small reaction, 17 (Fig. 1, C). Speaking broadly, it is unusual for cases giving such small reactions to respond well to digitalis, and thus the reaction carries prognostic significance.

On the other hand, patients with rheumatic mitral disease developing auricular fibrillation with rapid pulse rate, give large atropine reactions, normal or above (Fig. 1, A). Thus Table II, observations Ia, Ic, IIa, IIIa give reactions of 40, 50, 36, and 28 respectively, that is, practically normal or above. Silberberg had 4 patients who under similar circumstances gave reactions of 44, 53, 60, and 53. Thus, we see different cases, or groups of cases, give widely varying reactions under atropine. The pulse rate, the vagal influence being abolished, depends upon the activity of the pace-making part of the heart, that is, it depends upon either stimulus production or conduction. Just which is probably



incapable of proof, however, Silberberg's explanation seems more likely. He looks upon the bundle as being highly irritable in these fibrillating hearts with rapid pulse rate, and as carrying an excess of stimuli from the disorderly auricle to the ventricle. Thus a large atropine reaction probably means an irritable bundle, a small reaction some defect in the bundle.

Now let us turn to the role the atropine reaction may play in the study of the action of digitalis on the heart. First of all, let us briefly enumerate a few of the well recognized facts concerning the therapeutic action of digitalis. Digitalis produces the most decisive slowing of the pulse in those cases of old rheumatic mitral diseases which have developed auricular fibrillation, especially with rapid pulse rate. Digitalis has but little influence on hearts the seat of senile cardiosclerosis, especially with a slow pulse, even though they develop auricular fibrillation.

Patients with a regular rhythm rarely show any such marked response as the first group above. Of course, it is recognized that digitalis may produce a slowing in these cases, but never is the therapeutic effect so brilliant as in the first group. Now the question arises, how does digitalis slow the heart, especially in these cases of auricular fibrillation where the response is so decisive. The possibilities are: Increased vagal inhibition, sinus slowing, depressed conductivity (blocking), and possibly a direct nutritional influence on the whole heart. That is, it must act through the vagus, or on the heart itself, influencing some or all of its functions.

Prof. Cushny suggested that the atropine reaction might be used to eliminate the vagal factor in the digitalis slowing, and thus determine whether it is a large, a constant, or a varying factor. To determine this Silberberg studied 12 cases, mostly auricular fibrillation, in the Mt. Vernon Hospital, and the writer has a few to add.

The patients, having been in the hospital long enough to eliminate the possibility of drug influence from medicines taken before admission, on rest alone, had their atropine reaction taken according to the method described. They were then put on a good preparation of digitalis, usually the tincture, minims 15 to 20, three times a day, and kept on it until they showed their limit of tolerance, anorexia, headache, nausea, and possibly vomiting. Now the reaction was taken again and the results compared.

The group of cases of auricular fibrillation (Table II, Ia, Ic, II, III) show marked slowing under digitalis. A study of the pulse tracings of this group (Fig. 2) shows how the digitalis slowing is produced. Many small beats disappear, the remaining are more even in height, and the diastolic pauses more regular. Turning to the tracings of this same digitalized group when given atropine we find that many of the small beats reappear at the expense of the diastolic pauses as the pulse accelerates. The type in both

instances remains that of auricular fibrillation. The inference is that under digitalis increased vagal influence has prevented many

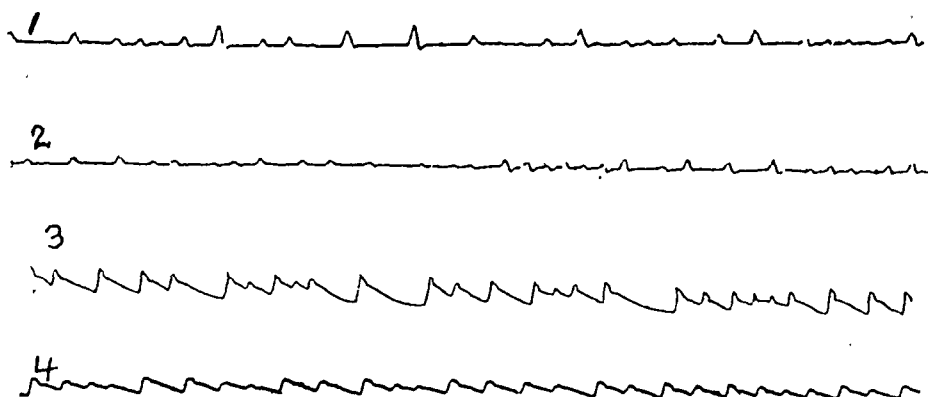


FIG. 2.—Showing character of pulse tracings in auricular fibrillation, Case III, Table II. Unfortunately, unintentionally the tracings of the patients giving larger reactions were destroyed. 1, before any treatment, pulse rate 90; 2, twenty minutes after injection of atropine, grain  $\frac{1}{25}$ , pulse rate 126; 3, full digitalis (drugs 34); pulse rate 55; 4, forty minutes after injection of atropine, grain  $\frac{1}{25}$ ; pulse rate 86; patient under full digitalis.

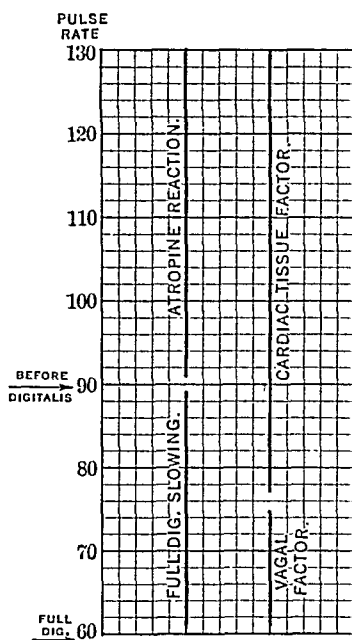


FIG. 3.—Silberberg's diagram adapted to Case I, Table II. The initial pulse before any treatment except rest was 90, and under atropine rose to 130. He was given full digitalis, and his pulse fell to 61. While under full digitalis the reaction was again taken but the pulse rate increased only from 61 to 75, a reaction of 14 which is the vagal factor in the digitalis slowing. Then 130 minus 75 or 55 represents in figures the increment of improvement in the cardiac muscle or the cardiac tissue factor.

stimuli from getting through. Remove this vagal influence by atropine, and again the fibrillating auricle sends through a rabble of impulses. Again we note in this group under atropine in digitalis

action the pulse rate not only does not reach the height attained under atropine before digitalis was given, but falls short of even the initial rate before any treatment whatsoever. If the vagal factor were the only element in the slowing we should expect to see the atropinized pulse rate reach the same height after digitalis, as it did before. Hence, there is evidently a second factor concerned in the slowing, which is probably the direct result of the digitalis on the heart itself, or the bundle, and is probably nutritional. These factors have been referred to as the vagal factor and the cardiac tissue factor. Their relationship will be most easily understood by referring to Fig. 3. These factors vary in different cases. The following tabulation will make the matter plainer:

Case.	Ia	Ic	II	III	IV	V	VI
Full vagal effect . . . . .	40	50	36	28	18	19	30
Full digitalis slowing . . . . .	29	32	57	36	0	35	0
Vagal factor . . . . .	14	12	1	29	0	64	40
Cardiac tissue factor . . . . .	55	70	92	35	18	0	0

In the first 4 cases the tissue factor is by far the greater. This is in accordance with their clinical history, their cardiac tissue was capable of great improvement under digitalis. They are the cases which get well enough to resume at least a part of their ordinary activity. Case II had a bundle most susceptible to digitalis which easily produced blocking. Case IV is typical of the experience with the well developed cardiosclerosis case. They can be promised little improvement under treatment. Case V, a patient in Dr. Sailer's service, showed the average slowing, but it was entirely vagal. He showed no improvement under atropine used therapeutically, nor under digitalis, and succumbed later with dilated heart and pulmonary edema. Case VI was the only post-pneumonic patient available at the time. His sound heart and normal pulse argued that digitalis would have no effect as it proved, but the toxin of pneumonia did not impair his response to atropine as it did in the typhoid cases.

CONCLUSIONS. 1. The atropine reaction in the normal heart is probably from 30 to 40.

2. A reaction of 20 or less, in a heart not recently subjected to exhausting disease, points to a degenerative process in the cardiac tissue which makes the outlook for improvement under treatment unpromising.

3. Cases of auricular fibrillation with responses normal or above are promising subjects for treatment.

4. Two atropine reactions in cases of auricular fibrillation, one before and one on full digitalis, enable us to determine whether the vagal or the cardiac tissue factor is the greater. The patients with a large cardiac tissue factor are the ones who usually are sufficiently improved by treatment to return to their occupations.

## THE THERAPEUTIC USE OF TUBERCULIN: A WORKING HYPOTHESIS AND SOME PERSONAL OBSERVATIONS.<sup>1</sup>

BY LAWRASON BROWN, M.D.,

SARANAC LAKE, NEW YORK.

WHEN I contemplated presenting to you my experience with tuberculin, my memory carried me back to the time some twelve years ago when I first began to use tuberculin under Dr. Trudeau's direction and inspiration. It is needless for me to say that I doubt if I would have begun its use at that time unless his faith had been so sure and strong that it was of some benefit. In 1900 Koch's original tuberculin had been in use nine years and his new tuberculin (T. R.) was some three years "old." Many modifications had already been tried: Hunter's, Trudeau's, etc.; Brehmer and Hahn had described their tuberculo plasmin and Klebs had learned at that time that antiphthisine did not fulfil his expectations. In 1900 I gave T. R. and a year later tuberculol of Landmann, a powerful poison which killed even normal guinea-pigs. The next year Koch described bacillary emulsion, and before long we were using that form of tuberculin. Since then I have used other forms of tuberculin, the broth filtrate, endotin, Beraneck's, old tuberculin, and mixtures of some of these forms.

To use any therapeutic means intelligently, to obtain its best results, and to advance the treatment of the disease by its exhibition, we should have in mind some reason for the faith that leads us to use it. I claim no originality for many of the following views which I have gathered from many sources, nor am I unaware that many objections, and some well founded, may be raised to these views, but they have afforded me a working hypothesis and as such I give them.

A WORKING HYPOTHESIS. It is a well-known fact that normal animals do not react to tuberculin, and show, even after repeated doses, no sensitiveness to it as indicated by the ordinary tuberculin tests or reactions. The tuberculin reaction depends upon the presence of tuberculous tissue in the organism. The mere presence of dead or living tubercle bacilli in the body is not sufficient for a tuberculin reaction. The difference between normal and tuberculous animals lies in the fact that the latter possess tuberculous tissue, where is formed spontaneous tuberculin which in some way renders the animal sensitive to tuberculin. It is probable that normal animals possess no so-called receptors for tuberculin which is therefore inert when injected into their bodies.

<sup>1</sup> Read before the Section on General Medicine of the College of Physicians of Philadelphia, April 22, 1912.

These receptors, or antibodies, are probably first formed in the focal (epithelioid) cells of the tuberculous tissue, cells which owe their formation to the irritation of the tuberculous poison and would seem therefore to possess from the beginning receptors for the poisons that have called them into existence. These cells are phagocytic and ingest tubercle bacilli, some of which they break down. What part the serum plays in setting free the protein portion of the tubercle bacilli, which is the active constituent of tuberculin, cannot be determined. It is this tuberculous protein, this primary protein as we may call it, that in all probability, sensitizes the body cells and is found in greatest concentration in the tubercle.

At this stage we might consider that the tubercle is composed of focal (epithelioid) cells, which contain tubercle bacilli in all stages of disintegration, primary protein and primary protein which has been acted upon by complement, either through the agency of some intermediary substance or possibly alone. This secondary substance, which if we like we may call anaphylatoxin, is what is concerned with the general and febrile reaction. The central nervous system and the tuberculous foci are most sensitive to this poison which often produces marked depression without general reaction or the usual fever. This explains what happens in many chronic cases, when without much fever and without apparent reaction they gradually lose weight and falling into a state of malnutrition, die finally from asthenia. The primary tuberculous protein is capable of sensitizing or stimulating cells in other parts of the body through, I believe, some agency arising in the tubercle. We may call it receptor, antibody, or amboceptor to facilitate discussion. Arising first in tuberculous tissue in the focal cells, these antibodies are in greatest concentration in the focus but later in the course of the disease are formed in other parts of the body. It is probably through these antibodies or amboceptors, that the injected tuberculin and complement are drawn into or fixed in the focus, thus producing focal reaction. Complement may be present in such small amounts that some time must elapse before a sufficient amount is fixed to produce the local reaction. In certain methods of application (cutaneous and ophthalmic tests) the amount of tuberculin absorbed depends, *cæteris paribus*, upon the time the tuberculin is in contact with the skin or conjunctiva. If, as occurs in the subcutaneous injection of tuberculin, only a small fraction of it is fixed at the site of injection, the remainder is absorbed into the circulation.

These receptors are most numerous in the focus whither most of the injected tuberculin finally finds its way and is fixed by the receptors. The period of incubation, the time between the injection of tuberculin and the general reaction depends upon the time required to bring enough injected tuberculin and tuberculin

in the focal cells together with the antibody and complement to set free sufficient anaphylatoxin to cause the general reaction. The union in the focus produces the focal reaction which brings about the hyperemia.

In tuberculin treatment the quantity of tuberculin injected usually falls short of the quantity necessary to enable the complement to set free sufficient anaphylatoxin to produce a general reaction but does cause a focal reaction. These focal reactions stimulate the formation of antibodies some of which are thrown off into the blood stream. In a few cases they occur spontaneously, but more often they are found only after larger doses of tuberculin. Termed usually antibodies, they may be said to include agglutinins, precipitins, bacteriolysins, opsonins, and complement deviating substances (antituberculin), etc. These substances, however, have not yet been causally connected with clinical improvement, or indeed, with sensitiveness to tuberculin. When large doses of tuberculin are reached without reaction, that is, tuberculin tolerance is acquired, it is possible that some of the free antibodies may partially neutralize the injected tuberculin, so that larger doses are required to produce reaction in even the most acutely sensitive cells of the tuberculous foci, while the cells in other parts of the organism, needing a greater stimulus to produce a response, fail entirely to react. This "neutralization" of tuberculin may rest only in part upon the presence of antibodies, and may depend more upon the increasing lytic activity of the complement. By this I mean that the splitting of the tuberculous protein may be so great that the stage of anaphylatoxin is entirely passed over, which probably occurs during pancreatic digestion of protein. It may again be explained by the failure of the complement to split up the primary protein (the injected tuberculin) which then calls forth a superabundance of antibodies or amboceptors, which would lead later, with an efficient complement, to the more intense disintegration of the tuberculin. It is also of interest to note that in some patients, when tuberculin is beneficial, it seems to bring about improvement in symptoms almost with the first dose.

Now focal reactions may lead on the one side to absorption of tuberculous tissue, due no doubt to the greater blood supply there present at that time, an idea which is based upon Bier's work on the effect of hyperemia upon chronic inflammation. On the other side, they may produce demarcation, softening, and destruction of the focus, which in turn may lead to deposition of lime salts or replacement by fibrous tissue.

The failure of tuberculous individuals to react to tuberculin may be due to the neutralization of the injected tuberculin by the presence of antibodies in the body juices, or again to the failure of the body to produce complement in sufficient amount to cause

reaction, or rather to the production of complement which is not sufficiently lytic to split up the injected tuberculin.

Hypersensitiveness is difficult to explain. The facts are that after an overdose of tuberculin the patient may become extremely sensitive to greatly reduced doses. This would indicate either an increased formation of the split product of the tuberculin anaphylatoxin, or increased susceptibility of certain cells of the body to the poison. Now patients who are doing well clinically, as well as some with active or subacute symptoms, may both present this phenomenon, which appears therefore to be favorable as well as unfavorable. An increased formation alone of anaphylatoxin would account for its unfavorable action, but this alone can hardly be the only cause, for it must also be increased in the favorable cases. Here the immunity mechanism seems so adjusted that whatever spontaneous primary protein escapes from the focus is immediately disintegrated, that is, the lytic process, set up by the complement, is so active that anaphylatoxin is never formed, and the lysis carries the splitting process on to the formation of simpler bodies. Now when a sufficient amount, however small, of tuberculin (primarily protein) is injected into the body, it changes this favorable balance and the action is not carried on so far and anaphylatoxin results. If perchance through overexertion a focus is flooded or washed out by an increased blood flow, so much more primary protein than usual escapes that it cannot be split up beyond anaphylatoxin, general and focal reactions occur and recur, which today some call excessive auto-inoculation. To stem these is at times difficult, and their result is disastrous.

It has been held that tuberculin does not act like other proteins, such as serum or egg white, in the production of anaphylaxis. A minute quantity of horse serum, injected into an animal previously sensitized with it, produces anaphylactic symptoms. The second injection may be introduced in any way and anaphylaxis results. This is not true of tuberculin. When, for instance, a normal guinea-pig is sensitized with a small quantity of tuberculin, enough, for example, to produce a skin reaction in a tuberculous guinea-pig, which is 0.02 c.c., and a second small dose is injected into the skin, muscles, or peritoneum, nothing results. If, however, a larger dose is injected, or if a very small dose is injected into the cerebral cavity or intravenously, anaphylactic symptoms supervene.

Recent work has shown that serum is the most concentrated form of protein solution that we have. Attempts to concentrate the primary protein of the tubercle bacillus lead to the conclusion that the greater dilution of this protein may explain many of the differences in action between it and serum. There is, however, a further difference that must be noted. To bring about tuberculin anaphylaxis, strong concentrations of tuberculin must be brought in direct contact with the cells of the central nervous system.

**THERAPEUTIC ADMINISTRATION.** Turning now to the practical therapeutic administration of tuberculin, I might repeat what I said six years ago, namely, that the most important point in the tuberculin treatment is the dosage. At that time I predicted that the opsonic index would never be generally adopted as a guide to the individual dose. Since that time the cutaneous and ophthalmic tests have been widely employed, and some have made use of them in determining the individual dose, as I shall mention a little later.

Many sites of administration of tuberculin have been employed, such as the oral, rectal, vaginal, intratracheal, intravenous, cutaneous, intracutaneous, subcutaneous, and the inhalation methods. For one reason or another, the majority of these have been discarded, and tuberculin is now usually injected under or into the skin. The intravenous method has some possibilities, but Koch and his followers who made use of it were never very enthusiastic about it and few have employed it.

**PREPARATIONS FOR ADMINISTRATION.** How long tuberculin retains its strength in solution has never been determined. Strong solutions (7.5 per cent.) appear to retain some of their reacting powers at the end of two to three years. Weaker solutions may deteriorate much more quickly, and I have used dilutions, freshly prepared, every two weeks. As a diluent,  $\frac{1}{4}$  per cent. phenol in physiological saline has been used, but the phenol can be replaced by lysol. A 10 c.c. cylindrical graduate, an ordinary tuberculin syringe, and a bottle of sterile physiological salt solution, preferably with a syphon or a stop-cock inserted at the side, enable one to make the dilutions in a very few minutes. Each dilution is  $\frac{1}{10}$  the strength of the preceding.

The skin should be rubbed with alcohol and the needles sharpened each day before use. A very fine needle should be used.

**VARIETIES OF TUBERCULIN.** The forms of tuberculin which I have used might be grouped under three heads:

1. Those forms of tuberculin which consist of extracts of tubercle bacilli or substances secreted during their growth, if such exist. Koch's original tuberculin is the best example of this class. Among other forms I have used Landmann's tuberculol, Denys's broth filtrate, Beraneck's tuberculin, tuberculin A. F., Gabrilowitch's endotin.

2. Tuberculin composed of the body substance of the tubercle bacillus, of which I have used T. R. and B. E.

3. I believe I was the first to suggest the use of these two types of tuberculin together. A compound known as B. F. Co. consists really of a mixture of broth filtrate and bacillary emulsion in the proportion of 5 to 2 by volume. This form of tuberculin contains every product of the tubercle bacillus, unaltered by heat and theoretically appeals to me very much.



Practically, I might say that I have not noticed any difference in the action of the various types of tuberculin save that some are more poisonous than others.

**DOSAGE.** When I first began to give tuberculin in 1900 I used the doses advocated by the makers of the various tuberculins which I employed. Accordingly, for O. T., the first dose was 0.1 mg. ( $\frac{3}{1}$ ), for T. R., 0.002 mg. ( $\frac{5}{2}$ ),<sup>2</sup> and for B. E. 0.0025 mg. ( $\frac{5}{25}$ ) solid substance. Later it seemed to me that when much smaller beginning doses ( $\frac{3}{1}$  or even  $\frac{3}{1}$ ) were employed, the patients reacted to much smaller quantities of tuberculin. Anaphylaxis had not been described at that time, but certainly many patients seemed to exhibit marked susceptibility to very minute doses. More recently I have again employed larger beginning doses, and frequently give 0.000001 or even 0.00001. These doses cause no reaction in many patients, but a few become hypersensitive, and I am never able to increase the dose very much.

**METHODS OF ADMINISTRATION.** There are two methods of giving tuberculin which have different aims in view. The usual method, that described by Koch and modified by Trudeau and others, is to give a dose much below that required to produce a reaction, and by gradually increasing the quantity, to bring about immunity or better, tolerance, not to the tubercle bacillus, but to tuberculin itself. I have employed this method for years, but always realized that it fell far short of what was required for the most successful treatment. When the discovery of opsonins was announced I hoped that the opsonic index would give us the criterion that we needed to select at each injection the optimum dose. It is needless for me to say that the method presents too many difficulties, too many uncertainties, to enable it to be employed for such purposes. In many patients it is not difficult to bring about a marked tolerance to most tuberculin, and there is some evidence to show that patients who take tuberculin well have a tolerance to it which may have been established before tuberculin treatment had been begun. One patient recently received as an initial dose, 0.00001 ( $\frac{4}{1}$ ) B. F., and in one hundred and fourteen days was given 33 doses, the last being 1000 mg. of B. F., without suffering a reaction or inconvenience at any time. The patient did very well, but was it on account of tuberculin? I question it. Others started about the same time have never been able to take a dose as large as this. They have not done so well.

Where tuberculin tolerance is wished, it seems to me safe to give, say  $\frac{1}{1}$  O. T. in 0.1 c.c. of diluent, intradermically, and to increase the dose tenfold twice a week ( $\frac{7}{1}$ ,  $\frac{6}{1}$ ,  $\frac{5}{1}$ ,  $\frac{4}{1}$ ) until the local skin reaction begins to be marked. In one case with extensive

<sup>2</sup> " $\frac{5}{2}$ " represents a convenient abbreviation for 0.000002 g. or c.c.  
VOL. 144, NO. 4.—OCTOBER, 1912. 18

physical signs, good general condition, and few symptoms, I reached a subcutaneous dose of  $\frac{3}{4}$  O. T. in six to seven weeks with only fairly marked intradermic reactions. Such a patient has a large number of highly sensitized areas in his skin which may possibly throw off antibodies into the blood. The beginning dose may in most cases be much higher without fear of reaction. Such a method would quickly lead to doses that cause response in the organism, and so bring about the formation of antibodies which occur more often with large than with small doses.

The rate of increase of the dose early interested me as I found that when I increased the dose by tenths of a cubic centimeter of the various dilutions (each of which is always ten times the strength of the preceding) I frequently obtained reactions when I increased from 1 to 2 or from 2 to 3 tenths. This led me to interpolate  $1\frac{1}{2}$  and  $2\frac{1}{2}$  tenths and to drop out 7 and 9. Later, with the aid of the late Mr. Pope, I constructed a logarithmic scale in which the increase was by geometrical proportion. This was based upon Fechner and Weber's law, namely, to increase the reaction in arithmetical proportion it is necessary to increase the stimulus in geometrical proportion. This table enables me to increase the dose from 0.01 to 1 c.c. of any dilution, using any rate of increase that I wish to select from 300 per cent. down to 12 per cent. I usually employ a rate of increase of 50 per cent. and find reactions no more likely to occur at one point of the scale than another.

The intervals are usually three or four days for the smaller doses and seven days for the larger doses.

The second method of giving tuberculin depends upon repeating the same dose at much longer intervals. Wright was the first to suggest such a method of treatment. I confess that I have never used the opsonic index method for it appeared to me from the start as impracticable. Good results have been reported by this method but Wright early stated that auto-inoculation was so frequent and so easily produced in pulmonary tuberculosis that his method was of little avail. On the other hand, Kinghorn and Twichell showed when an attempt was made to attain tuberculin tolerance, irrespective of the opsonic index, and the dose given in either the negative or the positive phase, the results were about the same. The opsonic index they concluded could be disregarded when tuberculin tolerance was aimed at. Many of us who have given tuberculin have, from time to time, received accidental inoculations which resulted in severe reactions. After recovering from such a reaction many experience a pronounced feeling of well being, which is so marked in some patients after the tuberculin test, that they have requested me to give them the tuberculin treatment. Such facts led W. C. White to attempt to estimate for each patient the dose of tuberculin that will just fall short of a fairly marked reaction. He makes use of the cutaneous

test and applies a definite quantity of tuberculin to an abrasion made so deep that the pink of the corium can be seen without producing any exudation of serum or blood. He then covers the tuberculin with a vaccination shield and allows it to dry *in situ*. When the cutaneous reaction at the end of the forty-eight hours has not exceeded 5 mm. he calls it the desired reaction and proceeds to give this dose, not subcutaneously, but in the lower layers of the skin where it causes a local or "Stichreaktion" of 20 to 40 mm. in diameter. If given oftener than every two weeks, he believes the patient acquires tolerance for tuberculin and so his interval is two weeks. I cannot subscribe to all the details of this method but in certain cases it is of apparent usefulness.

I shall not attempt to go into any details about increasing the dose when tuberculin tolerance is the aim. A good general rule is never to increase the dose when there has been any pronounced deviation from the usual trend of the disease. Another rule is when in doubt about giving an increased dose, do not do so. A very curious thing is that when tuberculin helps a patient very much, small doses appear to have as beneficial effects, certainly upon the symptoms, as larger. Tuberculin treatment, whatever working hypothesis is adopted, must be looked upon as a method of active immunization. Since this is the fact, it is useless to expect body cells, already flagging, to react with an adequate response. At such periods, tuberculin treatment should be omitted.

THE RESULTS. The goal of treatment in every patient is the cure of his disease or the alleviation of his symptoms. The estimation of the results of such treatment, however, is not always easy, for in many instances at least two personal equations enter, that of the patient and that of the physician. I am convinced that the explanation of the excellent results reported, for example, in pulmonary tuberculosis by the use of such substances as urea, sanosin, lignosulphite, griserin, nucleic acid, hetol, etc., are due far less to the action of the drug *per se* than to the effect of suggestion on the patient, perhaps unconsciously exerted, through the faith of the physicians who have first employed them. Certainly most of them when given as it were "in cold blood" produce such poor results that their use has been largely discontinued. Tuberculin cannot escape this weakness and indeed I believe its value can be greatly enhanced when the administrator has implicit faith in its curative properties and imparts that faith to his patients. The scientific physician of today who keeps faith with himself and refuses in such chronic and relapsing diseases as pulmonary tuberculosis to promise a "cure" to any patient by the use of any means, will certainly divest that means of a certain amount of suggestion and may rob it of some results that an absolute believer could impart to it. Such a believer, however, can get no idea how much of the results are due, for example, to tuberculin and how

much to the faith he has imparted to his patients. However, I am not here to discuss suggestion or auto-suggestion but the effect of tuberculin. I might say that the only suggestion I employ in connection with tuberculin is auto-suggestion by the patient. I try to be frank with him and tell him at the outset that tuberculin may help him and will not harm him if properly given, for of this I feel sure. One of my friends, whose faith in tuberculin is such that he can I believe honestly promise his patients that he will cure them with it, should get far better results than I, though he has never as yet collected his results.

Another factor which must be taken into account in discussing results of tuberculin treatment is the closer relationship that such treatment establishes between patient and physician. I must confess that I find it difficult to bring a patient to my office twice a week for months and discuss symptoms and fears, one of which gradually grows less while the other is often replaced by more or less indifference, borne of familiarity. When, however, I give this patient tuberculin, he and I can discuss his case in detail twice a week and I am able to discover slight but important changes in his condition, to check imprudence, and to change needless timidity into confidence in his ability to order aright his life. I cannot but believe that such a patient has a very great advantage over another who takes no such treatment. These factors must be taken into account in any treatment and I am convinced affect materially the results.

**THE EFFECT UPON SYMPTOMS.** The symptomatic effect of tuberculin demands careful study and observation during treatment. Much work has been done upon the blood. It was early stated that tubercle bacilli were mobilized and occurred in the blood during the tuberculin reaction, but trustworthy evidence has never been produced that such is the case. The leukocytes show an essential increase, rarely over 10,000 per cubic millimeter and Arneth's neutrophilic picture may be shifted to the right and so approach nearer normal. In some instances, especially after large doses, agglutinins, precipitins, opsonins, and complement deviating substances occur in the serum. The urine may show a diazo reaction at the height of a general tuberculin reaction but does not do so otherwise. Some believe the quantity of urine is increased. The weight may decrease slightly after large doses and especially after reactions but when the course is finished the weight often increases rapidly. The appetite is usually unaffected except with reaction, but may be improved. The strength is quickly affected when the doses are too large. A feeling of discomfort, of ill-being, even malaise, may occur without rise of temperature. They indicate tuberculin poisoning and must be avoided. When the temperature varies from 99° to 100° F., following each dose it may be lowered or fall to normal. In other patients a slight temperature

of 99.5° F. becomes normal and remains so but in a few rises again when treatment is stopped. Rise of temperature may not occur until the patient is severely poisoned with tuberculin and must not be considered the sole guide to dosage.

The localizing symptoms may be increased or diminished according to the effect of the dose. The cough and expectoration may be lessened with each dose in such a way that the patient calls attention to it. Such a dose should always be repeated as long as such favorable results are obtained. In others the cough and expectoration increase with each dose and the treatment has to be abandoned. Usually there is no effect noticeable one way or the other. The virulence and morphology of the tubercle bacillus are apparently unaffected, but more patients taking tuberculin seem to lose their bacilli. This is especially true for the moderately advanced patients. Oppression in the chest is not uncommon, while pleurisy can rarely be attributed to tuberculin.

The physical signs may be increased, but it is more often difficult to detect during treatment any change in the physical signs other than what usually occurs from day to day in most patients.

My experience leads me to believe complications occur less frequently among patients receiving tuberculin treatment, but it does not exclude their occurrence.

**THE UNTOWARD RESULTS.** Tuberculin, like arsenic or strychnine is a powerful poison which, when used injudiciously, is capable of great harm. The disrepute into which tuberculin fell at first was due to the selection of patients who should never have received it and to faulty dosage and too short intervals. Coincidence undoubtedly accounts in part for some of the so-called "unfortunate results." The mobilization of tubercle bacilli in the body, claimed by some to occur after tuberculin, has never been proved to occur either clinically or experimentally. In over 10,000 injections, 11 instances of hemoptysis more or less closely connected with or at least following tuberculin (in one to three days) have come under the writer's notice. In none was it severe, in most slight, and in 8 a previous hemoptysis had occurred. I have given, together with my assistants, to some 200 to 300 patients from 10,000 to 20,000 injections and have observed but two unhappy results at the site of inoculation. In one, a patient received too large a dose of bacillary emulsion at a single point and developed a sterile abscess which was healed by aspiration without opening. The second patient had what seemed to me to be a neuritis, as there was little to be seen at the site of inoculation. It was exceedingly painful and prostrating and deterred me for many years from injecting tuberculin into the arm. I might add that I now nearly always give it in the arm.

I have seen patients taking tuberculin do badly and have seen complications arise which might be attributed to it. I have also

seen the same complications occur in patients to whom we had thought of giving tuberculin. While I have tried to keep an open mind in regard to tuberculin, I may be somewhat prejudiced in its favor, though many of my colleagues in Saranac Lake would more readily believe the opposite. Consequently, when I say I have never seen any permanent untoward results to be attributed directly to tuberculin, I hope you will believe that I have tried to be fair.

There is some evidence, both experimental and clinical to show that tuberculin may cause nephritis, or at least, that it develops during treatment.

**EXPERIMENTAL RESULTS.** The results of treatment of tuberculous animals with tuberculin has not been satisfactory. Life has been prolonged and changes have occurred in the lesions which demonstrate an attempt at healing but cure or bacterial immunity has not been effected. Some deny the value of animal experimentation in regard to tuberculin in man and much slipshod work has been published. Today the value of tuberculin treatment for man rests largely upon the results obtained in man.

**ULTIMATE RESULTS.** The results in man have been for the most part good but many observers have failed to support their contentions with proof other than their personal belief or impressions.

Selection of patients certainly affects the results, and when only favorable cases with tubercle bacilli in the sputum are chosen, the results will be far better than when all patients are given the treatment. At the Adirondack Cottage Sanitarium we gave tuberculin to carefully selected patients for a time and then selected for a year or two the worst cases. Later we exercised no selection but allowed the patients to elect to take tuberculin treatment. We thought this would be the fairest test but in reality it has resulted in a selection against tuberculin as those patients who wished to stay a little longer because they were more advanced or ran a subacute course chose to take tuberculin. The patients we selected because they were the worst, did remarkably well. The results on the whole, when reduced to cold figures, with every error we could think of eliminated, showed that among the moderately advanced patients those who took tuberculin did better than those who did not, while for the incipient stage the difference was less pronounced. This held true for both immediate and ultimate results.

In the individual case, however, tuberculin often falls far short of what is hoped from its use. In early cases it is almost impossible to say how much good tuberculin does. In the more advanced cases favorable results are more often seen and in the very chronic cases the effect of tuberculin is in a few truly astonishing, so good, in fact, that no one questions it. It is these results that win for tuberculin its advocates and I am sure that after two or three

such cases few would doubt its efficacy in some patients. When, however, results are tabulated and impartial statistical methods applied, they are so far from upholding the impressions created by these few cases that the statistical methods themselves, and not the results of tuberculin, are questioned.

My observation leads me to believe that incipient cases treated with tuberculin do somewhat better than those not so treated, while the moderately advanced cases do much better. The ultimate results do not show such marked differences, but indicate that the treated, both incipient and moderately advanced, do better.

---

## REST VERSUS CLIMATE IN THE TREATMENT OF PULMONARY TUBERCULOSIS.<sup>1</sup>

BY WILLIAM C. VOORSANGER, M.D.,

VISITING PHYSICIAN TO MOUNT ZION HOSPITAL; CLINICIAN TO SAN FRANCISCO TUBERCULOSIS  
CLINIC, SAN FRANCISCO, CALIFORNIA.

THE world is still knocking at the door of the medical profession asking for a cure for its greatest scourge, and we who are particularly interested in the treatment of pulmonary tuberculosis are certainly anxious to unite upon some sane rational therapy pending the discovery of a true specific.

Phthisiotherapists agree upon but one point, namely, that tuberculosis is curable. Their mode of procedure in effecting this cure varies to a considerable degree. As an example of this, two years ago I was able to collect 75 varieties of tuberculin in the market, each with its champions and devotees, claiming some particular merit for their special brand, seemingly forgetful of the fact that tuberculin is a product of the tubercle bacillus, call it by what name you will, and that success in treatment depends not so much upon the form used as upon its dosage and mode of administration.

So has it been with other measures for the treatment of tuberculosis as its therapy has evolved through the centuries from Hippocrates and Aretaeus, who knew little about it, down to Robert Koch, who has given us our present-day conception of the disease. Climatic treatment ruled supreme for many years, and particularly in the United States. It became the rule when a patient was pronounced tuberculous to send him to another climate—warmer, drier, higher, or lower—than his own. Colorado, California, Arizona, and New Mexico became the favored resorts, the four

<sup>1</sup> Read at the Seventh International Tuberculosis Congress held at Rome, April 14 to 20, 1912.

Meccas to whose shrines thousands of misdirected tuberculous individuals have gone, the major portion of whom never returned.

In the majority of cases the doctor is responsible for sending his patient away from home, either from a belief that another climate will benefit him or because (which unfortunately is too often the case) his own therapeutic resources are at an end and he wishes to put the responsibility of the death of his patient upon someone else. I wish to state emphatically that I consider it criminal to send an advanced case of tuberculosis away from home under the delusion that another climate will cure him. Any physician of the Pacific Coast, and particularly we in California, can bear testimony to having seen innumerable cases of advanced tuberculosis, sent by their physicians, for whom absolutely nothing could be done. Let us once for all put every personal or material consideration aside and come out boldly for this principle: That climate *per se* plays but a very small role in the present-day treatment of pulmonary tuberculosis. Most of us believe this, some still doubt, some still have faith in the high altitude treatment, some in the dry air climate, some in a change from any climate to any climate.

I can readily understand that a climate which has a maximum amount of sunshiny days in the year will prove more cheerful to a patient than one where it constantly rains. Upon this ground alone can I see much merit in change of climate. Where a patient is depressed and firmly convinced that he cannot get well a change of scene and a brightening of his surroundings may become important. But the unqualified transference of tuberculars from one climate to another without individualization is bad therapeutics.

We see more tuberculosis in California than in any part of the United States with the possible exception of Colorado, which proves that physicians do not yet recognize the truth that climate unaided never did and never will cure tuberculosis. A considerable proportion of the fairly advanced cases, which I see in both clinical and private practice is composed of patients who have been to one or more sanatoria for a cure. This certainly must be the experience of other physicians in California interested in tuberculosis and goes to prove that the tubercular who cannot be cured at home cannot be cured elsewhere, other things being equal. Why do we still constantly persist in the blunder of making a fetish of climate, imbuing the mind of the sufferer with its almost supernatural influence, and as a result causing him to live uncontrolled and unadvised, always getting worse but believing the contrary? To remedy this error medical men must be convinced that tuberculosis, particularly the pulmonary form, is a disease of metabolism, a disease of cell destruction, a disease of tissue waste, a disease where bacteria are locked up in bronchioles, generating toxins, and that our only chance of arresting this devastation is to stimulate the natural defences within the body, the antibodies. Climate cannot



do this. All the grand results attributed to climate in the past have been due to open air, food, and the control within a sanatorium. Air is air whether high or low, and can be obtained in any climate. The open air and sanatorium treatment must be distinctly differentiated from so-called climatic treatment. If you send cases to a distinct locality for the purpose of getting care, proper medical attention, and better facilities than can be obtained at home no fault can be found. But the physician first and the patient secondly must learn that in treating pulmonary tuberculosis we are attempting to stop waste; we are attempting to check toxemia; we are striving to put the body in such condition that the introduction of artificial toxins will stimulate its natural defences and form a maximum amount of antibodies. Only in this way do I believe we will be able to create out of the experience of the past a rational tuberculosis therapy.

At the last Tuberculosis Congress, Williams, of London, covered these points most ably by stating "that the history of consumption has ever shown that more has been accomplished by measures which augment and reinvigorate the resisting powers of the sufferer than by measures which aim at destroying or rendering harmless the invading tubercle bacillus."

Sewall, of Denver, in a recent article on open air, concluded that there was no existing proof that the increase of carbon dioxide, the decrease of oxygen, or the addition of organic animal matter under ordinary circumstances could prove deleterious to health. Air cannot destroy the effects of the tubercle bacillus primarily. Air simply does its share in stimulating metabolic change.

Osler has said that a man with beginning tuberculosis may fight a winning battle if he lives out of doors in any climate whether high, dry, cold, low, moist, or warm.

What then becomes our duty in the treatment of a curable case of pulmonary tuberculosis? As I see it after struggling with the problem for several years, tempering personal experience and failure with the experience and failures of others, it is plainly to build up a faulty metabolism and if possible produce an immunization. For my own guidance I have tabulated tuberculosis therapy as follows, each heading in its relative degree of importance: (1) Rest; (2) diet; (3) open air; (4) tuberculin therapy; (5) climate.

I am firmly convinced and shall try and prove my position by the record of results which are given later that rest is our most important therapeutic agent in the treatment of pulmonary tuberculosis. Brehmer was the first to introduce a system of graduated exercise into the treatment of tuberculosis. His work has been augmented and improved upon by Paterson at the Brompton Sanatorium, Frimley. Latham also in treating his patients insists upon rest and graded exercise as the best therapeutic agent for reducing fever and toxemia and controlling the danger of auto-inoculation.

We all recognize the value of open air for twenty-four hours daily if possible. We sanction caloric feeding, which means not overfeeding, not forcing the organism to assimilate beyond its power, but sufficient feeding to restore body-weight to normal. In a particular individual most of us believe in tuberculin therapy, the conviction gradually becoming fixed that it will some day become a true specific, but we are not all ready to accept the doctrine of the importance of rest applied scientifically. Formerly a patient was told "to go west and rough it." For this reason the physician on the western coast of the United States has been able to see so many cases of tuberculosis. Those who come west and rough it uncontrolled seldom get well. Often, too, we see the arrested case breaking down through overstrain.

Rest means freedom both from physical and mental strain. Rest should be applied in fairly accurate dosage just as we figure out diet in calories and our tuberculin in milligrams. It is not sufficient to tell the patient to take plenty of rest and not to walk too much, and not to engage in mental worry or work. The number of hours of rest *per diem* should be prescribed, and if mental strain is present the doctor should acquire the patient's confidence, learn its nature, and if possible remove it.

Again, the importance of graduated rest and exercise in administering tuberculin cannot be too strongly dwelt upon. Tuberculin reactions, failure to acquire arrest or retrogression of a tuberculous process may often be attributed to our forgetting that auto-inoculation goes on continually within the body of the tubercular, that tuberculin itself is being produced, and that antibodies are being generated. If we are ever to obtain an immunity in tuberculosis it can only be by creating a proper balance, that is, by administering the toxin (tuberculin) for the purpose of supporting and stimulating the natural defences already in the body, the antibodies. Any scientific theory which has been developed, whether the Arloing and Courmont agglutinin theory, the Bordet and Gengou antibody theory, or the antituberculin hypothesis of Wassermann and Bruck, cannot overcome the truth that tuberculin can only become the true specific of the future if we realize that we do not inject antibodies, but stimulate those already in the body.

Following the experience of Nathan Raw,<sup>2</sup> with bovine T. R. I began injecting my cases with bovine tuberculin, and in October, 1910, reported<sup>3</sup> 28 cases, of which 15 were apparently cured or arrested. I consider this result most satisfactory and attributed it to the greater efficacy of the bovine tuberculin over the human form in the treatment of pulmonary tuberculosis.

I have continued in the exclusive use of this form of tuberculin and can now report 210 cases in which the results have practically

<sup>2</sup> Lancet, February 10, 1903.

<sup>3</sup> California State Jour. Med.

been as good as in the original 28. But I have changed my viewpoint somewhat, and although still believing that bovine tuberculin is the toxin of choice in the treatment of tuberculosis caused by *Bacillus typus humanus*, I must attribute my results primarily to the enforced rest to which all my patients are subject. We err if we do not appreciate that tuberculosis with fever is like any other disease with fever, the result of bacilleemia and toxemia and should be treated with rest in bed, that tuberculosis with emaciation is like any other devastating process and needs rest; that tuberculosis with weakness is like myocardial weakness and needs rest if we are to acquire proper functional restitution.

In order to prove the assertion that rest is the most important agent in our therapeutic armament for fighting tuberculosis, I have procured records from most of the large sanatoria upon the Pacific Coast and in Colorado, in order to compare them with my own results obtained in San Francisco. The directors of the various sanatoria were written to and the results as herein given (see Table on p. 540) are taken from their personal statements.

In a comparison of the results obtained by various observers in their respective localities as shown in the following table some facts stand out rather prominently. The greatest percentage of apparent cures has been obtained by the Pottenger Sanatorium and the National Jewish Hospital at Denver; the greatest percentage of arrests by the Colfax School for the Tuberculous; the Barlow Sanatorium at Los Angeles, and myself; the greatest number of improvements by the Walter Henry Memorial Sanatorium at Seattle and the United States Naval Hospital at Las Animas, Colorado, and the United States Army Hospital at Fort Bayard, New Mexico. The altitude of the two last named sanatoria are respectively 3800 and 6100 feet and the absence of successful result (cures and arrests) is accounted for by the fact that most of the cases at Fort Bayard are chronic, being discharged tuberculars from the United States army, and a great many sent to Las Animas are advanced. The two sanatoria are situated in regions once thought to possess absolute curative climatic power, and the altitude of Fort Bayard is the highest of any locality mentioned in the table with the exception of Fort Stanton. This should prove sufficiently that climate cannot influence materially a tuberculous process and that a tuberculous patient who cannot get an arrest at home cannot obtain it elsewhere.

The Pottenger Sanatorium, situated at a comparatively low altitude (1000 feet) above sea level and with a wide range of temperature, shows the best results. Dr. Pottenger does not attribute his success to climate but to "all measures which aid in building up and nourishing the body, such as open air; good food; the careful adaptation of rest and exercise; suitable baths and medicinal tonics; to the end that the cells will be as responsive as possible; then furnishing the toxin necessary to stimulate the cells to the

Place.	Altitude. Feet.	Range of temperature.	Capacity of bed.	No of cases 1910-1911.	Apparently cured. Per cent.	Disease arrested. Per cent.	Improved. Per cent.	Unimproved. Per cent.	Died. Per cent.
Burlew Sanatorium, Los Angeles, Cal.	330	94° to 30° F.	40	59	9 (15.59)	21 (35.59)	11 (18.64)	10 (16.95)	8 (13.56)
Pottenger Sanatorium, Monro- via, Cal.	1000	109° to 31° F.	100	About 200	Beginning Advanced Average 12 ( 2.76)	cases 80 30 55 17 ( 3.91)	Not given	Not given	Not given
United States Army Hospital, Fort Bayard, New Mexico	6100	102° to 30° F. below zero	400	435	23 (16.00)	26 (18.00)	178 (40.7)	177 (40.7)	50 (11.7)
United States Army Hospital, Fort Stanton, New Mexico	6200	83° to 21° F.	250	144	28 (13.10)	20 ( 9.40)	23 (16.0)	28 (19.4)	41 (28.4)
United States Naval Hospital, Las Animas, Colorado	3800	103° to 20° F. below zero	238	213	6 (17.60)	9 (26.10)	82 (38.5)	50 (23.4)	33 (15.5)
Union Printers' Home, Colorado Springs, Colorado	6035	94° to 15° F.	54	34	52 (23.20)	49 (21.80)	11 (32.3)	8 (23.5)	7 ( 3.1)
National Jewish Hospital, Denver, Colorado	5280	100° to 29° F. below zero	130	224	6 ( 4.70)	39 (30.40)	33 (14.7)	79 (31.2)	8 ( 6.2)
Colfax School for the Tuberculous Colfax, Cal.	2420	107.5° to 32° F.	50	128	.....	5 ( 5.50)	35 (27.5)	40 (31.2)	64 (64.1)
Maricopa Hospital, Arizona . .	1300	118° to 28° F.	25	99	1 ( 2.10)	2 ( 4.20)	5 ( 5.5)	15 (16.5)	10 (21.0)
Walter Henry Memorial Sanato- rium, Seattle, Wash.	300	86° to 22° F.	31	48	31 (14.70)	74 (35.20)	22 (45.8)	13 (27.0)	35 (16.7)
San Francisco (Author) . . .	18	49.2° to 87° F.	..	1909-1911 210			34 (16.2)	36 (17.1)	

\* Dr. Pottenger would not segregate his cases, stating that he averaged about 80 per cent. of cures and arrests in beginning cases and about 30 per cent. in advanced cases. This would make an average of 55 per cent. apparent cures and arrests.

production of protective substances as is done by intelligently employing tuberculin." He also lays great stress upon individualization, stating that "no physician can obtain the best results unless he can see something beyond tuberculosis and recognize the fact that tuberculous patients are drawn from the mass of human beings, hence liable to all the ills of un-tuberculous individuals."

Dr. M. Collins, in charge of the National Jewish Hospital for Consumptives at Denver, states: "I consider results obtained to a large degree due to our climatic conditions as well as to the *care, discipline, and attention* which our patients receive in the hospital itself." His apparent cures were 23.2 per cent.; arrests, 21.8 per cent. At Fort Stanton, New Mexico (United States Army Hospital), Dr. F. Smith in charge states that various degrees of importance are attached to the climate of this particular locality by different men. Fort Stanton shows 16 per cent. of apparent cures and 18 per cent. of arrests, while Fort Bayard for chronic cases in practically the same locality shows only 2.7 per cent cures and 3.9 per cent arrests. Dr. Smith in a recent publication states "sometimes a change is either unnecessary or useless, and moreover a climate adapted to the needs of one individual may be wholly unsuited to those of another." The Barlow Sanatorium, which shows apparent cures 15.25 per cent. and arrests 35.59 per cent. through its superintendent, Dr. R. L. Cunningham, makes this statement; "I do not consider this locality as favorable as certain places in Arizona or New Mexico and even some points of California on the desert," and still the Barlow Sanatorium shows better results than the Maricopa Hospital in Arizona, the Fort Stanton Hospital in New Mexico, or the Peers School for the Tuberculous at Colfax.

Dr. Peers, of Colfax, a careful observer, attributes his results to change of climate, freedom from fog and contaminating organization, and ability to live the outdoor life without discomfort 365 days in the year.

Now, to compare the above results with my own in 210 cases, treated at practically sea level, some in a sanatorium but the majority at home, ambulant. Before doing so I wish to make one observation: A just comparison can only be made if apparent cures and arrests are grouped, because we naturally all have different ways of construing results and what one dubs an apparent cure another may call an arrest. Personally, I am careful how I list a case as cured, since many of my cases which at the end of treatment were symptomless have relapsed in from six months to one year. I have also treated many cases which have been discharged from various sanatoria as cured. We all know the inaccuracy of statistics, and only by following our cases can our reports be exact. All the cases here reported have been under observation at least three years, and with but few exceptions their conditions at the present time are known. In the attempt, therefore, to be as conservative as possible,

I can report of 210 cases, apparently cured, 14.7 per cent.; arrested, 35.2 per cent.; total, 49.9 per cent., practically a 50 per cent. successful result in a series in which the cases were not selective but taken at random from all classes of people. Tabulating together apparent cures and arrests from the various places under discussion we have: Barlow Sanatorium, 50.8 per cent.; Pottenger Sanatorium, 55 per cent.; United States Army Hospital at Fort Bayard, 6.67 per cent.; United States Army Hospital at Fort Stanton, 34 per cent.; United States Army Hospital at Las Animas, 22.5 per cent.; Union Printers' Home, Col. Springs, Col., 43.23 per cent.; National Jewish Hospital, Denver, Col., 45 per cent.; Colfax School for the Tuberculous, Cal., 35.1 per cent.; Maricopa Hospital, Arizona, 5.5 per cent.; Walter Henry Memorial Sanatorium, Seattle, Wash., 6.3 per cent.; Author (San Francisco), 49.9 per cent.

A survey of this grouping will show that my results are practically as good as those obtained at other places despite the fact that the climate of San Francisco has always been regarded as impossible for the cure of tuberculosis. To be sure, the net result in any report of cases will depend largely upon the number of advanced cases handled, but I feel certain that my present series contains as many advanced cases as the majority of sanatoria in the statistical table. This is demonstrated by a death rate in the series of 16.7 per cent., with no improvement in 17.1 per cent.

I am convinced that climate today plays the least important role of any of our therapeutic aids to the treatment of pulmonary tuberculosis. The fact is becoming more and more evident that the war against tuberculosis must be waged by each community within its own borders and not as heretofore each community shirking responsibility by making some other its dumping ground. Relapses are most common in patients who have received a cure in one climate and who attempt to live in another. Consequently, a tubercular should live in the climate in which he has been cured which must naturally be his home climate.

We must not deceive ourselves in believing that the therapeutic millenium of tuberculosis has arrived, and that we can absolutely cure it. We none of us know how many of our cures or arrests will stand the test of time.

In conclusion, this much I want to set forth with positiveness. If climate shall in future be disregarded and communities develop phthiotherapists who in their own climate will build up a faulty metabolism of their patients through rest, open air, and proper feeding in order to, with the aid of tuberculin, stimulate the generation of antibodies within the body, a long step forward will have made in the therapy of tuberculosis.

I wish to express my thanks to the various directors and superintendents of the sanatoria and institutions above mentioned who have so willingly and kindly assisted me in making this report possible.

## DIABETES MELLITUS AND TUBERCULOSIS.

BY CHARLES M. MONTGOMERY, M.D.,

INSTRUCTOR IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; PHYSICIAN TO THE HENRY PHIPPS INSTITUTE, UNIVERSITY OF PENNSYLVANIA, AND THE WHITE HAVEN SANATORIUM.

THE association of diabetes mellitus and tuberculosis has been the subject of unusual interest during the last half-century. Richard Morton's<sup>1</sup> cases of diabetes associated with wasting (tabes) described in the seventeenth century were not cases of tuberculosis judging from the description of the cases. John Rollo,<sup>2</sup> in his book on diabetes, published in 1798, manifests no special interest in this subject, though he gives the clinical and postmortem records of a case of diabetes evidently complicated by pulmonary tuberculosis with cavity formation. The credit for the first report of a large number of diabetic cases, with special reference to tuberculosis of the lungs, belongs to Griesinger (1859), who records 250 cases. Windle, in 1883, reported the autopsies of 333 diabetic patients, with mention of the pulmonary conditions. Following Koch's discovery, in 1882 (see authorities cited by H. Fink<sup>3</sup>), tubercle bacilli were found in the sputum and lungs of diabetic patients (1883), and tuberculosis was produced in animals by inoculation with the sputum. Tuberculosis complicating diabetes has even been found in animals. Schindelka<sup>4</sup> reported pulmonary tuberculosis in a diabetic dog, and Berenger-Férand observed cerebral tuberculosis in a monkey. The interest in the two diseases has largely been directed toward the frequency of tuberculosis in diabetes and the various causes supposed to explain this frequent complication.

ANALOGIES BETWEEN TUBERCULOSIS AND DIABETES. A number of authors have been impressed with certain points of similarity between tuberculosis and diabetes. Thus Sauvage<sup>5</sup> speaks of the interference with nutrition in the two diseases, the abundant elimination of waste products in the urine, both organic and mineral, and the diminished respiratory activity. Shively<sup>6</sup> points to the progressive course in both diseases, to the emaciation, to the great fatality in early life, and the better resistance in later life, to the strong racial affinities, to their greater prevalence in cities than in the country, and to various other conditions common to both tuberculosis and diabetes. Purdy<sup>7</sup> states that the "terri-

<sup>1</sup> Phthisiologia, 1694. English translation.<sup>2</sup> Cases of the Diabetes Mellitus, London, 1798.<sup>3</sup> Münch. med. Woch., 1887, No. 37.<sup>4</sup> Cited by B. Naunyn Der Diabetes Mellitus, 1906, p. 152.<sup>5</sup> Paris Theses, 1895.<sup>6</sup> New York Medical Journal, May 16, 1908, p. 933.<sup>7</sup> Diabetes Mellitus, 1890. p. 14.

tories furnishing the highest mortality from diabetes in the United States coincide very closely with those furnishing the highest mortality from consumption. The very frequent termination of diabetes in consumption lends significance to this fact."

**DIABETES AND TUBERCULAR HEREDITY.** A few writers have been impressed with the frequency of a family history of tuberculosis in diabetic patients. Thus, Croner<sup>8</sup> relates the occurrence of an hereditary or family tendency to tuberculosis in 37 out of 100 diabetics, 12 more of whom were themselves tubercular. He cites Schmidt, who believes there is a diabetic predisposition or diathesis in tuberculous families. Among 48 cases of diabetes collected by the writer only 2 had recorded a definite tubercular family history, and 6 more a questionable family history of tuberculosis, but the completeness of these records in regard to family history cannot be vouched for. Even Croner's figures are not especially remarkable when compared with the great prevalence of tuberculosis.

**GLUCOSE AS AN ETIOLOGICAL FACTOR IN PREDISPOSING DIABETIC PATIENTS TO TUBERCULOSIS.** The assumed predisposition of diabetics toward infection with the tubercle bacillus has been explained most frequently on the hypothesis that glucose outside of the body exerts an especially favorable influence on the growth of these organisms. Glucose added to a number of culture media, for example blood serum and bouillon, exerts as favorable or nearly as favorable an influence on the growth of tubercle bacilli as does the more commonly used material, gelatin (Eastwood<sup>9</sup>). In comparison to blood serum, however, glucose, whether added to blood serum or other media, never has an influence on the development of tubercle bacilli greatly beyond that of blood serum alone, and toward some strains of the tubercle bacillus has an even less favorable influence than the normal blood serum. Whatever especially favorable action has been found for the action of glucose has been the result of using glucose in strengths of 5 per cent. or more, while in the blood of diabetic patients the amount rarely reaches 1 per cent.—a proportion attained by only one patient in the literature<sup>10</sup> reviewed by the writer. Handmann's<sup>11</sup> experiments are the only ones I have found in which small quantities of glucose (0.5 to 1 per cent.) were added to normal blood. He states that this amount of glucose does not render it any better culture medium for staphylococci, nor does it lower the bactericidal action toward these organisms, and does not lessen the normal opsonin in the blood serum. There is equally little evidence to support Honl's<sup>12</sup> claim that the growth

<sup>8</sup> Deutsch. med. Woch., 1903, xxix, 821.

<sup>9</sup> Second Interim Report, Royal Commission on Human and Animal Tuberculosis, London, 1907, Part II, Appendix, vol. iv.

<sup>10</sup> B. Naunyn, *Der Diabetes Mellitus*, 1906, p. 188.

<sup>11</sup> Deutsch. Archiv f. klin. Med., 1911, cii, 1.

<sup>12</sup> Wien. klin. Rundschau, 1898, xii, 245, 265, 299.



of the organisms of mixed infections is promoted by the glucose in sufferers from diabetes. The animal experiments of Budjwid,<sup>13</sup> in which he injected dogs hypodermically with suspensions of bacteria in 12 to 25 per cent. glucose solutions, and of Preyss<sup>14</sup> and Leo,<sup>15</sup> who investigated the development of tuberculosis in animals rendered glycosuric through phloridzin, shed no light on the subject. Some writers (see C. von Noorden<sup>16</sup>) believe that the high glucose content of the blood in diabetes results in injuries to the tissues that predispose them to infection.

Bernheim and Dieupart<sup>17</sup> make an interesting report on tuberculosis in the working people of a certain sugar factory. In a dispensary in the neighborhood of the factory 150 cases of tuberculosis were observed among 1500 employees, women being affected more frequently than men. The writers attribute the great frequency of the disease less to the chemical influence of the sugar than to the mechanical injury to the bronchial mucous membrane produced by the sharp sugar dust. Most of the employees in the sugar factory showed serious injuries to the teeth. The writers state that exactly as in the case of diabetes, tuberculosis with the working people of the sugar factory takes a rapid course, and is always fatal.

**LOSS OF WEIGHT.** Loss of weight either on its own account or because of various conditions causing it is often stated to predispose the individual to tuberculosis, and particularly the diabetic patient in whom the wasting may be extreme. Simple lack of nourishment is commonly considered to favor the development of tuberculosis, but as it is apt to be associated with poor surroundings and unusual opportunities for exposure to the tubercle bacillus, infection cannot be excluded as the chief or only cause of the disease in many of these poorly nourished persons. Among non-tuberculous persons of subnormal weight living under better conditions there is no positive demonstration that tuberculosis develops with unusual frequency. Experimental work on animals has shed little light on the effect of insufficient feeding as a cause for tuberculosis, most of the experiments failing to exclude all abnormal factors except the reduced diet. Preyss<sup>18</sup> noted no appreciable effect on the development of tuberculosis in underfed animals. In many chronic affections accompanied by loss of weight, there is no special tendency for the development of tuberculosis, for example, pernicious anemia (Cabot<sup>19</sup>), leukemia (Osler), exophthalmic goitre (Dock),<sup>20</sup> and various malignant diseases. Among wasting diseases having tuberculosis as a fre-

<sup>13</sup> Centralbl. f. Bakteriologie u. Parasitenkunde, 1888, iv, 577.

<sup>14</sup> Münch. med. Woch., 1891, xxxviii, 418.

<sup>16</sup> Die Zuckerkrankheit, 1910, p. 165.

<sup>18</sup> Münch. med. Woch., 1891, xxxviii, 418.

<sup>20</sup> Ibid., vi, 377.

<sup>15</sup> Zeitschr. f. Hygiene, 1889, vii, 505.

<sup>17</sup> Tuberculosis, Berlin, 1908, vii, 194.

<sup>19</sup> Osler's Modern Medicine, iv, 625.

quent complication, cirrhosis of the liver has been especially emphasized by Osler<sup>21</sup> and Kelly,<sup>22</sup> and others, but the mortality from tuberculosis complicating cirrhosis of the liver does not appear particularly remarkable when compared to the general tuberculosis mortality.

**MISCELLANEOUS ETIOLOGY.** Of the many other causes offered to explain the alleged hypersusceptibility of diabetic patients to tuberculosis, only a few will receive passing mention. Thus "diminished vigor," "lessened resistance," "metabolic disturbances with excessive elimination and deficient absorption interfering with nutrition" (Sauvage), the presence in the body of various poisonous substances, atrophy and inflammation of the respiratory passages (Blumenfeld<sup>23</sup>), and various other conditions are supposed to favor the development of tuberculosis in diabetics. However, neither the facts nor the reasoning furnished in support of these alleged causes are convincing, and most of the explanations are little more than plausible, being often the result of *post hoc, propter hoc* reasoning, whereby the frequency of tuberculosis in diabetes is explained by the various abnormal conditions associated with diabetes.

**EVIDENCES INDICATING A PARTICULARLY ACUTE PROCESS IN TUBERCULOSIS COMPLICATING DIABETES.** In support of the idea that diabetes predisposes to tuberculosis, it has been urged that the tuberculosis often pursues a very brief course in diabetes and at autopsy frequently reveals an acute process. West<sup>24</sup> mentions 50 diabetic cases studied post mortem in which 21 were tuberculous, 4 of these presenting the lesions of chronic tuberculosis, while in the rest phthisis was active and the cause of death. Dreschfeld<sup>25</sup> speaks of an acute tuberculous broncho-pneumonia occurring in diabetes, running a more rapid course than ordinary phthisis, and being characterized by an early and very extensive formation of cavities. Babcock<sup>26</sup> likewise supports this view. Undoubtedly tuberculosis is one form of terminal infection that frequently attacks the diabetic. Out of 355 autopsies on diabetic cases collected from the literature and postmortem records, 138 showed pulmonary tuberculosis, mostly acute. This subject is dealt with further under Clinical and Pathological Aspects of Tuberculosis in Diabetes

**HEMATOLOGICAL STUDIES RELATING TO ETIOLOGY.** Particularly interesting are the results of Da Costa and Beardsley,<sup>27</sup> who found in diabetics a lowered opsonic index toward the *Staphylococcus pyogenes*, the *Streptococcus pyogenes*, and the tubercle bacillus.

<sup>21</sup> Practice of Medicine, 1896, p. 476.

<sup>22</sup> Therap. Monatshefte, February, 1899.

<sup>23</sup> Diseases of the Organs of Respiration, 1902, ii, 523.

<sup>24</sup> Medical Chronicle, Manchester, 1884-85, i, 5.

<sup>25</sup> AMER. JOUR. MED. SCI., September, 1903.

<sup>26</sup> Osler's Modern Medicine, v, 779.

<sup>27</sup> Diseases of the Lungs, p. 197.

Studies on the resisting powers of the blood have also been carried on in depancreatized dogs. Sweet<sup>28</sup> found that after removal of the pancreas in dogs there was a complete loss of bactericidal power in the blood toward *B. coli communis*, *B. typhi abdominalis*, and *B. dysenteriae*. Thomas and MacPhail,<sup>29</sup> found that the opsonic index curves for *Micrococcus aureus* regularly declined in all depancreatized dogs. Nebelthau,<sup>30</sup> on the other hand, found no differences in the development of tuberculosis in depancreatized and control dogs. But in the experiments with depancreatized dogs the interval until the time of their death was always too short, never over six and usually within three weeks, to make a fair comparison between occurrences in these animals and in human beings the subjects of diabetes.

Raw<sup>31</sup> has conducted some suggestive experiments, too few to carry weight, to show the effect on the growth of the tubercle bacillus on artificial media through the addition of blood from a diabetic patient.

**FREQUENCY OF TUBERCULOSIS IN DIABETES.** The frequency of tuberculosis as a complication of diabetes has greatly impressed nearly all writers on this subject except von Noorden and Cornet, it being apparently assumed that this frequency considerably exceeds the general tuberculosis mortality. This conclusion, doubtless, largely results from using general hospital statistics like those of Adami and McCrae,<sup>32</sup> who found only 17.3 per cent. of tuberculous cases (after excluding all healed and latent cases) in 1000 autopsies, and from failure to use figures expressing the general tuberculosis mortality. Thus, one-third of all deaths in persons aged between fifteen and forty-four years, according to Baldwin,<sup>33</sup> are due to tuberculosis. Cornet's<sup>34</sup> figures for Prussia in the decade 1881 to 1890 show that between the ages of fifteen and sixty years the tuberculosis mortality varied according to age and sex between 25.1 and 46.6 per cent. According to the United States Census Report for 1909 the number of deaths from tuberculosis of all forms "per 100 deaths from all known causes at each age" in the registration area was as follows:

Age . .	Under 10	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	Over 90
Per cent.	3.4	26.1	37.0	29.3	18.6	10.4	5.3	2.5	1.0	0.0

Conclusions, moreover, are unreliable if based on figures obtained previous to the discovery of the tubercle bacillus; for instance, the figures of Griesinger (1859), who in 250 diabetics

<sup>28</sup> Jour. Med. Research, 1903-4, v, 255.

<sup>29</sup> Monthly Cyclopedia and Medical Bulletin, September, 1911, p. 535.

<sup>30</sup> Arch. f. exper. Path. u. Pharmak., 1901, xlix, 384.

<sup>31</sup> Tuberculosis, Berlin, May, 1911.

<sup>32</sup> Sixth International Congress on Tuberculosis, v. I, pt. I, 325.

<sup>33</sup> Osler's Modern Medicine, iii, 143.

<sup>34</sup> Tuberculosis, 1904, p. 277.

states that tuberculosis occurred in 42 per cent. of the cases and was the cause of death in 39 per cent. Bouchardat (1875) claims to have found tuberculosis in all of 19 autopsies on diabetic patients, and Windle<sup>35</sup> found that more than one-half of 333 autopsies on diabetic subjects "presented the changes of the disease or group of diseases known as phthisis." Among other points affecting the reported frequency of tuberculosis in diabetes are the stage and degree of activity and the accuracy of diagnosis of the tuberculosis, the age of the patients, and the stage of the diabetes.

**FREQUENCY OF TUBERCULOSIS IN DIABETES.** Cases of Diabetes Non-fatal while under Observation: Writer's collected cases, 51; tuberculous, 0. Philadelphia Polyclinic Hospital Dispensary (Dr. Riesman), 10 cases; tuberculous, 0.

Cases of Diabetes in Which Mortality is Generally not Mentioned: R. T. Williamson,<sup>36</sup> 100 consecutive cases; tuberculous, 29 (14, signs of advanced phthisis; 14, slight signs at apices; 1, detected post mortem). Da Costa and Beardsley,<sup>37</sup> 50 cases; tuberculous, 10. W. Croner,<sup>38</sup> 100 cases; tuberculous, 12. F. M. Sanwith,<sup>39</sup> in Egypt, number of cases not mentioned; tuberculous, about 12 per cent. B. Naunyn,<sup>40</sup> 149 "pure" diabetic cases; tuberculous, 25. B. Naunyn, 103 diabetic cases resulting from demonstrable organic diseases; tuberculous, 8. N. Raw,<sup>41</sup> 62 diabetic cases, with 27 autopsies; tuberculous, 37 (2, abdominal tuberculosis).

**Fatal Cases:** (Autopsies not performed or not mentioned.) Writer's collected cases, 35 (none autopsied), pulmonary tuberculosis, 3. F. T. Frerichs,<sup>42</sup> 250 cases; pulmonary tuberculosis, 34.<sup>43</sup> C. von Noorden<sup>44</sup> (private cases), 292; tuberculous, 15 (pulmonary, 14; intestinal, 1). R. T. Williamson,<sup>45</sup> 42 cases; pulmonary tuberculosis, 6. R. M. Fitz<sup>46</sup> and E. P. Joslin, 20 cases; pulmonary tuberculosis, 3.

**Cases Autopsied:** Writer's collected cases, 25; pulmonary tuberculosis, 6; all active. F. T. Frerichs,<sup>47</sup> 55 cases; pulmonary tuberculosis, 21. I. Honl,<sup>48</sup> 29 cases; pulmonary tuberculosis, 12. H. Noltemius,<sup>49</sup> 20 cases; pulmonary tuberculosis, 4; all active. B. Naunyn,<sup>50</sup> 50 cases; pulmonary tuberculosis, 20; exclusive of old

<sup>35</sup> Dublin Jour. Med. Sci., 1883, lxxvi, 112.

<sup>36</sup> Diabetes Mellitus, 1898.

<sup>37</sup> Deutsch. med. Woch., 1903, xxix, 821.

<sup>38</sup> British. Med. Jour., October, 1907, p. 1059.

<sup>39</sup> Loc. cit.

<sup>40</sup> Ueber den Diabetes, 1884, p. 132.

<sup>41</sup> W. Fox (Diseases of the Lungs and Pleura, 1891, p. 551) and S. West (Diseases of the Organs of Respiration, 1902, ii, 523) wrongly quote Frerichs as recording 87 tuberculous cases among 250 diabetics.

<sup>42</sup> Loc. cit.

<sup>43</sup> Jour. Amer. Med. Assoc., July 23, 1898, vol. xxxi.

<sup>44</sup> Wien. klin. Rundschau, 1898, xii, 245, 265, 299.

<sup>45</sup> Beiträge zur Statistik u. pathologischen Anatomie des Diabetes Mellitus, Kiel, 1888.

<sup>46</sup> Loc. cit.

<sup>37</sup> Loc. cit.

<sup>41</sup> Loc. cit.

<sup>43</sup> Loc. cit.

<sup>47</sup> Loc. cit.

scars. S. West,<sup>51</sup> 50 cases; pulmonary tuberculosis, 21; (4 chronic, remainder active and cause of death). Reports of the Surgeon-General 1895-1905, 5 cases; pulmonary tuberculosis, 2. K. A. Heiberg,<sup>52</sup> 5 cases; pulmonary tuberculosis, 0. R. T. Williamson,<sup>53</sup> 24 cases; pulmonary tuberculosis, 12. J. Seegen,<sup>54</sup> 92 cases; pulmonary tuberculosis, 40. Total, 355 cases; pulmonary tuberculosis, 138 (38.9 per cent.).

Cases of Diabetes Showing Effect of Different Living Conditions: Dr. David Riesman, diabetic cases in private practice, 45; tuberculous, 1. C. von Noorden,<sup>55</sup> diabetic cases in private practice, number not mentioned; tuberculous, 5.5 per cent. Diabetic cases in public hospitals, number not mentioned; tuberculous, 15.1 per cent. Diabetic cases in Russian Jews, 45; tuberculous, 27 (60 per cent.).

The above tabulation illustrates well the frequency of tuberculosis in diabetes under a number of conditions. The tabulation with the autopsy figures gives the most reliable information, if it is borne in mind that these are probably all or nearly all hospital cases. The clinical cases vary in part with the carefulness and diagnostic skill of the physicians in charge. Thus, compare the writer's collected fatal but non-autopsied cases with those examined post mortem. Carelessness in diagnosis is particularly well illustrated by a febrile patient under constant and in many respects careful observation in a hospital for over eight months without there being found any abnormal condition in the lungs until the autopsy revealed extensive bilateral tuberculosis. The table on the effect of different living conditions is very instructive.

FREQUENCY OF TUBERCULOSIS IN DIABETES ACCORDING TO AGE. Available figures on the incidence of tuberculosis in diabetes according to age are unfortunately very meagre and do not demonstrate conclusively any variation in diabetics from non-diabetics. In children and old people tuberculosis is to be less frequently expected than in those of the intervening period. Sauvage<sup>56</sup> refers to 7 cases of tuberculosis in 42 diabetic infants. Wilcox<sup>57</sup> cites a number of authors who consider tuberculosis among the most frequent complications of diabetes in infants and young children, an opinion apparently not endorsed by Holt.<sup>58</sup> Williamson<sup>59</sup> believes that young patients who do not die at a comparatively early stage from coma or some intercurrent disease usually develop tuberculosis, especially if they are suffering from a severe form of diabetes. Von Noorden<sup>60</sup> found no cases of tuberculosis in 10 diabetics in the first decade of life, none out of

<sup>51</sup> Loc. cit.

<sup>52</sup> Loc. cit.

<sup>53</sup> Loc. cit.

<sup>57</sup> Archiv. of Pediatrics, September, 1908.

<sup>58</sup> Diseases of Infancy and Childhood, 1905, p. 1136.

<sup>59</sup> Loc. cit.

<sup>52</sup> Virchow's Archiv, May, 1911, cciv, No. 2.

<sup>54</sup> Der Diabetes Mellitus, 1893.

<sup>56</sup> Loc. cit.

<sup>60</sup> Loc. cit.

14 in the second, 2 cases of pulmonary tuberculosis out of 26 in the third, 3 out of 64 in the fourth, 4 out of 63 in the fifth, 5 out of 61 in the sixth, 1 of intestinal tuberculosis out of 49 in the seventh, and no cases of tuberculosis out of 2 diabetics in the eighth decade. The ages in the writer's 25 collected autopsies on diabetic patients are tabulated elsewhere.

THE FREQUENCY OF DIABETES AND GLYCOSURIA IN TUBERCULOSIS. Except for general statements to the effect that diabetes and glycosuria occur comparatively infrequently in tuberculosis, the literature has little to say on the subject. Richardson<sup>61</sup> writes, "On the whole, judging from experience, I should think that of 1500 cases of a phthisical character, not more than one would be a case of diabetic phthisis." Vibert<sup>62</sup> records 3 cases of glycosuria, usually slight, in 50 cases of tuberculosis. Abeles<sup>63</sup> found traces of sugar in 18 of 66 cases of far advanced tuberculosis.

The frequency of glycosuria and diabetes in the accompanying table is chiefly based on the reports from 25 tuberculosis sanatoria and hospitals in various parts of the United States. Out of 31,834 cases of tuberculosis there were 101 (about  $\frac{1}{3}$  of 1 per cent.) cases of glycosuria and 51 (about  $\frac{1}{6}$  of 1 per cent.) cases of diabetes. Some of the cases classed as glycosurics were undoubtedly diabetics, so that the percentage of diabetics may be assumed to be between  $\frac{1}{3}$  and  $\frac{1}{6}$  of 1 per cent. of all these tuberculous cases. From this table have been eliminated all sanatoria known to exclude diabetes or to fail to make urine examinations in all cases. The proportion of cases in the advanced stages of the disease is higher than the general average for all sanatorium cases in the United States. The autopsy figures show 5 cases of diabetes among 937 post mortems. It is possible that Adami and McCrae's cases of diabetes were admitted as diabetics and not as consumptives, as their report is based on general hospital cases and not on tuberculous cases which are all admitted primarily for their tuberculosis.

TUBERCULOSIS PRECEDING THE DIABETES. West<sup>64</sup> says that it is very rare for a patient with phthisis to develop diabetes mellitus. Raw<sup>65</sup> states that among 4000 cases of tuberculosis he cannot recall a single case with urine free from sugar on admission which developed diabetes mellitus. This has been the experience of the Phipps Institute and all sanatoria and physicians in communication with me on this point, except in regard to 2 or 3 cases reported to me as cases of primary tuberculosis, but unaccompanied by the data necessary to establish such a diagnosis. De Wolf<sup>66</sup> makes the general statement that the tuberculosis may be the primary disease. Shively<sup>67</sup> mentions a case which he considered developed

<sup>61</sup> Med. Times and Gazette, 1867, i, 219.

<sup>62</sup> Wien. med. Woch., 1874, p. 467.

<sup>63</sup> Loc. cit.

<sup>64</sup> Jour. Amer. Med. Assoc., 1883.

<sup>65</sup> Cited by Sauvage.

<sup>66</sup> Loc. cit.

<sup>67</sup> Loc. cit.

## THE FREQUENCY OF DIABETES IN TUBERCULOSIS.

State.	Town or post office.	Institution or physician.	No. of cases of pulmonary tuberculosis reported on	No. of cases of glycosuria.	No. of cases of diabetes mellitus.
Colorado	Denver	Agnes Memorial Hospital	2200	2	2
Colorado	San Animas	United States Naval Hospital	1195	0	0
Connecticut	Hartford	Hartford Hospital	500	2	2
District of Columbia	Washington	Tuberculosis Hospital	1300	4	?
Illinois	Naperville	Edward Sanatorium	550	2	2
Maryland	Baltimore	Baltimore Municipal Tuberculosis Hospital	1315	2	2
Maryland	State Sanatorium	Maryland State Sanatorium	1200	4	4
Massachusetts	Rutland	Rutland State Sanatorium	1291	5	?
Missouri	Mt. Vernon	Missouri State Sanatorium	648	0	0
Missouri	St. Louis	Dr. Boisliniere	1321	1	1
New Jersey	Glen Gardner	New Jersey Sanatorium for Tuberculous Diseases	1472	4	?
New Mexico	Fort Bayard	United States Army General Hospital	3188	5	2.
New Mexico	Fort Stanton	United States Marine Hospital Sanatorium	1884	11	4
New Mexico	Silver City	New Mexico Cottage Sanatorium	1050	5	5
New York	East View	West Chester County Tuberculosis Hospital	372	4	?
New York	Liberty	Workmen's Circle Sanatorium	245	0	0
New York	Loomis	Loomis Sanatorium	1338	7	3
New York	New York	Department of Health, Tuberculosis Sanatorium	2950	9	5
New York	Santa Clara	Hill Crest and Uplands	113	0	0
New York	Saranac Lake	Adirondack Cottage Sanatorium	340	0	0
North Carolina	Asheville	Winyah Sanatorium	1231	6	6
Ohio	Cincinnati	Cincinnati Hospital	1722	8	8
Pennsylvania	Philadelphia	Home for Consumptives	203	0	0
Pennsylvania	Philadelphia	Phipps Institute, University of Pennsylvania	3336	19	5
Pennsylvania	Pittsburg	Tuberculosis League	300	0	0
Wisconsin	Wales	Wisconsin State Tuberculosis Sanatorium	570	1	?
			31834	101	51

## AUTOPSIES.

	Pulmonary tuberculosis.	Diabetes mellitus.
Reports of the Surgeon General, Public Health and Marine-Hospital Service, 1895 to 1905 . . . . .	373	0
Henry Phipps Institute until end of 1910 . . . . .	479	1
Adami and McCrac, Pulmonary Tuberculosis with Cavity Formations <sup>63</sup> . . . . .	85	4
	937	5

<sup>63</sup> Loc. cit.

diabetes during pregnancy. I have entirely failed to meet with the record of a definite case of tuberculosis preceding diabetes, though one can hardly avoid assuming that this must take place at times. Healed and latent tuberculous lesions are being constantly encountered in cases of diabetes. In many cases it is impossible to tell whether the diabetes or the tuberculosis is the primary disease.

**DURATION OF THE DIABETES BEFORE THE ONSET OF THE TUBERCULOSIS.** This varies to some extent with the general conditions surrounding the patient just as does the mortality for tuberculosis. The age, the severity of the diabetes, and other factors also exert an influence on the development of tuberculosis in some cases. S. West asserts that tuberculosis does not, as a rule, appear in the acute cases of diabetes, and is rare in cases of less than two years' standing. Fox<sup>69</sup> says that tuberculosis commonly appears after the diabetes has lasted from one to two years. Purdy<sup>70</sup> considers that perhaps the majority of patients who have suffered from diabetes for more than two or three years are attacked by tuberculosis. Shively mentions 5 cases, in 1 of which the tuberculosis is said to have preceded the diabetes, while in the other 4 symptoms of tuberculosis developed eighteen, twelve, seven, and two months after the patients were known to be diabetic. In 3 cases collected by the writer in which the tuberculosis presented the appearances of a terminal infection the longest period preceding death after the detection of the first evidences of tuberculosis was three months and eleven days. Out of 17 cases from the records of the Hospital of the University of Pennsylvania, 6 gave a duration of the diabetes for periods of from five to seventeen years without any suspicion of tuberculosis.

**CLINICAL ASPECTS OF TUBERCULOSIS IN DIABETES.** Diabetes may be complicated by all types of clinical tuberculosis, but a certain number of the cases are characterized by symptoms disproportionately slight in comparison to the extent and acuteness of the pulmonary disease. This modification of symptoms occurs particularly in those cases of advanced diabetes developing tuberculosis as an acute rapid terminal infection. The enfeebled state of these patients, somewhat as in old people developing tuberculosis, partly explains this change in the symptomatology, but more important, at least in some of the cases, is the rapid progress of the tuberculosis with fatal termination before the evolution of the pathological processes necessary to the production of some of the tubercular symptoms, such as hemoptysis and the presence of tubercle bacilli in the sputum, which are more liable to occur in cases of longer duration. Instead of being actually masked or diminished, however, the symptoms may be overlooked because attention is concentrated on the diabetic condition while the lungs are entirely neglected. In 3 cases of acute extensive tuberculosis investigated by the writer,

<sup>69</sup> Diseases of the Lungs and Pleura, 1891.

<sup>70</sup> Diabetes Mellitus, 1890.



no localizing pulmonary symptoms were recorded in one, cough and pain were the first symptoms in a second, coming on three and one-half months before death, and pain was the first symptom in a third preceding death by one and one-half months. The temperature has frequently been noted to be normal or below the average for tuberculosis, partly as a result of the lowered temperature peculiar to many diabetics. Shively found 4 out of 6 cases of tuberculosis complicating diabetes to be afebrile, while the temperature of the other 2 never exceeded 100°. On the other hand, a considerable rise of temperature in all of 4 cases of active tuberculosis, 3 being very acute and extensive, was encountered by the writer. The cough may likewise be slight and delayed until near the fatal termination. The expectoration may be slight and has been recorded as absent in some cases.

**HEMOPTYSIS.** As in other symptoms of tuberculosis complicating diabetes, there is some difference in the experience of different observers as to the frequency of hemoptysis, though most clinicians have been impressed with its relative rarity. Von Noorden states that it occurs in about 12 per cent. of cases of tuberculosis complicating phthisis. Sanwith did not observe it in any of the cases coming under his notice in Egypt, and Williamson invariably failed to meet with it even in cases observed up until the time of death. Shively, on the other hand, found hemoptysis to be frequent and considerable in amount in 4 out of 6 cases. In 3 cases with extensive but acute tuberculosis of both lungs collected by the writer, there was no hemorrhage recorded, though the cases were observed in hospitals until the time of death.

**TUBERCLE BACILLI IN THE SPUTUM.** Tubercle bacilli appear in the sputum in large numbers according to Immerman and Rüttimeyer, but the majority of writers consider that they occur rarely or not at all (von Noorden). Von Noorden himself failed to find them in 4 open cases with copious sputum, and in a fifth (far advanced) case only after repeated search were a few tubercle bacilli found. In the lungs from this patient the cheesy nodules and their walls revealed masses of tubercle bacilli. Shively in 6 cases found tubercle bacilli present in 3 and absent in 3. In a patient in the wards of the University Hospital who had acute extensive bilateral pulmonary tuberculosis with cavity formation, tubercle bacilli did not appear, in spite of frequent sputum examinations and the use of methods to concentrate the bacilli, until a week before death, and then only a few were detected.

**SUGAR IN THE SPUTUM.** Bagou and a number of others report the presence of sugar in the sputum of tuberculous diabetics. Shively detected it in 1 out of 6 patients. Bussenius<sup>71</sup> detected sugar in the sputum in the proportion of 0.25 per cent.

<sup>71</sup> Cited by R. T. Williamson, *Diabetes Mellitus*, 1898.

**PAIN.** This subject is little if at all referred to in the literature, unless under individual case reports. In one case collected by the writer pain and cough were the first symptoms pointing to disease of the chest, both coming on three months and eleven days before death. Two days later friction rubs were audible. In another case of acute extensive tuberculosis, pain and cough developed about the same time, some six weeks before death.

**TUBERCULIN.** Sanwith<sup>72</sup> mentions 4 patients with diabetes complicated by tuberculosis, who received injections of Koch's tuberculin up to 10 milligrams. None of these reacted to the tuberculin, though 1 died suddenly of coma, and was proved at autopsy to have phthisis in the upper lobe of the right lung.

**SWEATING.** The effect of diabetes in lessening sweat secretion is asserted to occur even in the presence of tuberculosis. (Bagou.<sup>73</sup>)

**EFFECT OF TUBERCULOSIS ON DIABETIC SYMPTOMS.** It is a common opinion that tuberculosis may lessen certain of the symptoms of diabetes. Williamson records 3 cases of diabetes complicated by tuberculosis with disappearance of glycosuria within a few days to six weeks before death. "With this disappearance of sugar the thirst and diuresis also ceased, and the whole clinical aspect of the cases, in the last stage of the disease, gradually changed from diabetes to phthisis with marked wasting." Purdy<sup>74</sup> considers the disappearance of sugar in the course of the lung complication a consequence of pyrexia. Sweet,<sup>75</sup> in experimental work on animals found no evidence indicating a decreased excretion of glucose during an infection. Futcher<sup>76</sup> considers it not unusual in diabetes with pulmonary tuberculosis accompanied by high fever, to see the sugar almost entirely disappear in the terminal stages. In one case investigated by the writer the sugar which at one time had reached 10 per cent. fell to 4.3 per cent. nineteen days before death. This patient had a very extensive and rapidly fatal form of tuberculosis of the lungs, and the acetone almost disappeared. Diabetic coma has been regarded as a rare occurrence in tuberculosis. One case has been recorded by Williamson, one has been reported to me by Dr. Riesman, and one occurred among the writer's collected cases.

**PATHOLOGY OF TUBERCULOSIS COMPLICATING DIABETES.** The Lungs and Pleura: Pulmonary tuberculosis in diabetes may appear in all the forms seen in tuberculosis uncomplicated by diabetes, but in diabetes it is supposed to be specially liable to take the form of a very rapid and extensive, usually caseous, tuberculosis, with early cavity formation, and with no tendency to cicatrization. This occurred in 3 of the writer's 6 cases. Tuberculous pleurisy appears in all its forms in diabetes, though

<sup>72</sup> Loc. cit.

<sup>73</sup> Paris Theses, 1888.

<sup>74</sup> Loc. cit.

<sup>75</sup> Jour. Med. Research, 1903-4, v, 255.

<sup>76</sup> Diabetes Mellitus, Osler's Modern Medicine, i, 774.

considered rare by Renon.<sup>77</sup> Pneumothorax has been described and pleural effusion though not encountered by the writer in the literature, occurred once among his collected cases.

**The Larynx:** The literature furnishes little but general statements about laryngeal tuberculosis in diabetes. A patient of this sort is at present attending the Phipps Institute Dispensary.

**The Intestines:** Tuberculous ulcers were found in the intestines twice in 92 autopsies on diabetic patients reported by Seegen,<sup>78</sup> the lungs being tuberculous in 40 of the cases. Among the writer's 6 collected cases there was no case of intestinal tuberculosis.

**Meninges and Brain:** I have been able to find only two references to tuberculous involvement of these structures in diabetes, one Rokitansky's case of meningeal tuberculosis cited by Seegen, the other De Jonge's<sup>79</sup> case of tuberculous involvement of the medulla oblongata.

**The Liver:** Seegen records 2 cases of tuberculosis of the liver in 92 post mortems on diabetic subjects and 1 case out of 30 in Rokitansky's series.

**The Spleen:** Miliary tuberculosis of the spleen has been reported by Pagou in a case of general miliary tuberculosis complicating diabetes. A questionable diagnosis of tubercles in the spleen was made in one of the writer's cases.

**The Kidneys:** Seegen reports tuberculosis of the kidneys twice in 92 post mortems on diabetic cases, Williamson once in 20.

**The Adrenals:** A case of adrenal tuberculosis in a diabetic subject occurred in one of the writer's series. (Described in the *Jour. of the Amer. Med. Assoc.*, March 23, 1912, lviii, 847.) Ogle<sup>80</sup> describes a case considered by Naunyn<sup>81</sup> to be one of tuberculosis of the adrenals.

**The Peritoneum:** One case of general tuberculosis of the peritoneum occurred among the writer's cases of diabetes. None was found in the literature.

**The Lymph Nodes:** I have found no record of tuberculous adenitis in diabetes except a general statement by Lloyd<sup>82</sup> and one case in the present series which showed tuberculosis of the bronchial and mesenteric glands.

**Other Organs:** The bones are infrequently found tuberculous in diabetes to judge from general statements. No reference could be found to tuberculosis of the heart, pericardium, genital organs, skin, or pancreas in diabetes.

**ACUTE GENERAL MILIARY TUBERCULOSIS.** Bagou<sup>83</sup> has reported a case of diabetes with good clinical and pathological notes in which

<sup>77</sup> Arch. Gén. de Méd., Paris, 1903, i, 528.

<sup>78</sup> Cited by F. T. Frerichs, Ueber den Diabetes, 1884, p. 136.

<sup>80</sup> St. George's Hospital Reports, 1866, i, 178.

<sup>81</sup> Der Diabetes Mellitus, 1906, p. 55.

<sup>83</sup> Paris Theses, 1888.

<sup>79</sup> Der Diabetes Mellitus, 1893.

<sup>82</sup> Post-Graduate, 1906, xxi, 637.

the lungs, liver, and spleen were filled with miliary tubercles. It is considered by many to be a rare disease in diabetes.

**BACTERIOLOGY OF THE LUNGS IN TUBERCULOSIS COMPLICATING DIABETES.** Besides tubercle bacilli, which may be found in profusion in the lungs even when few or absent in the sputum, various other microorganisms may be associated with the tubercle bacillus. Honl<sup>84</sup> considers that tuberculosis complicating diabetes is usually a polymicrobial infection. Ehret<sup>85</sup> attaches much importance to the influence of secondary or mixed infections in the tuberculosis of diabetes. He believes that there is a more varied and more luxuriant growth of organisms than in uncomplicated tuberculosis.

**PROGNOSIS OF TUBERCULOSIS AND DIABETES.** To judge from the literature and from reports received from a number of sanatoria, the experience of many physicians has been that the association of tuberculosis and diabetes in the same patient offers a gloomy outlook, and some assert that it is practically always fatal. While admitting the greater seriousness of two diseases, one is struck with the number of cases in which the tuberculosis and the diabetes seem to pursue quite independent courses in the same individual, each responding to treatment or neglect, and each requiring a prognosis based entirely on its own merits. Von Noorden mentions a patient with pulmonary and laryngeal tuberculosis and 4 per cent. of sugar, whose sugar, with appropriate treatment, fell to 0.5 per cent., whose larynx became healed, whose expectoration ceased, and who was in good health nine years later. At present there is in attendance at the Phipps Institute a patient who was admitted a year ago with pulmonary and laryngeal tuberculosis and diabetes (sugar, 5.5 per cent., specific gravity, 1040) whose condition is at present quite satisfactory, the lung condition being almost arrested, though the amount of sugar has not greatly varied. Reports from a number of physicians based on experience in private practice and sanatoria has yielded 11 definite cases ending fatally, 1, however, in coma and not as a result of his tuberculosis. Of 3 not ending fatally, 1 improved temporarily and later was lost sight of, 1 improved in his pulmonary and general condition although the amount of sugar remained stationary, and the third case, in spite of a large amount of sugar, showed improvement in his tuberculosis and lost his sugar.

Important factors determining the prognosis of tuberculosis complicating diabetes are: (1) The condition of the patient, each disease having to be considered separately, and the combination also having to be estimated so far as possible; and (2) the use or neglect of appropriate treatment for each disease. Of particularly bad omen is the acute rapidly extending form of tuberculosis

<sup>84</sup> Wien. klin. Rundschau, 1898, xii, 245, 265, 299.

<sup>85</sup> Münch. med. Woch., 1897, xlv, No. 52.

coming on late in the course of diabetes, and behaving in the manner of a terminal infection. In many cases, however, the prognosis as to the tuberculous condition may be made at least tentatively along the same lines as in uncomplicated tuberculosis. The glycosuria is not aggravated by the tuberculosis. One should always think of the possible occurrence of tuberculosis as a terminal infection in diabetes. A number of French writers have stated that diabetes dependent on lesions of the pancreas usually ends fatally in tuberculosis in a comparatively short period, while the gouty (arthritic, constitutional, hereditary) type, as they call it, commonly showing 3 to 4 per cent. of sugar and often lasting twenty-five to thirty years, may resist tuberculous invasion for a long time. Sauvage considers that an excess of uric acid in the blood antagonizes the development of the tubercle bacillus. He adds that tuberculous patients improve on hyperalimentation with nitrogenous foods, and states that carnivorous animals are rarely affected and herbivorous animals are often affected with tuberculosis. This subject has recently been referred to by Raw, who says that the treatment of tuberculosis should aim at the production of an artificial gout.

**TREATMENT OF DIABETES COMPLICATED BY TUBERCULOSIS.** This important subject can only be very briefly alluded to here. While there are times when either the diabetes or the tuberculosis demands special treatment which ordinarily would be contraindicated for the other disease, the cases are fortunately comparatively few in which proper treatment for one of the diseases seriously interferes with successful results in the other. General tuberculosis treatment tends to help the diabetic by rendering him less liable to this form of infection. A diet providing a considerable proportion of milk and eggs is often well borne in both conditions. Every precaution should be taken by the diabetic patient to avoid the development of tuberculosis both from germs that may be harbored by himself, and from those he may be exposed to through his surroundings.

**SUMMARY OF CASES.** Out of 111 cases of diabetes collected in the hospitals of Philadelphia, 9 had active pulmonary tuberculosis, and 1 other had adrenal tuberculosis. Out of 51 non-fatal cases of diabetes, none had active pulmonary tuberculosis. Out of 60 fatal cases of diabetes, 9 had active pulmonary tuberculosis and 1 other had adrenal tuberculosis. Out of 35 fatal but non-autopsied cases of diabetes, 3 had active pulmonary tuberculosis. Out of 25 post mortems, 6 showed active pulmonary tuberculosis and 1 tuberculosis of the adrenal gland without tuberculosis elsewhere. Out of 86 non-autopsied cases (35 fatal) 3 had active pulmonary tuberculosis and 17 more had signs recorded that were only slightly suggestive of tuberculosis.

Physical signs in 86 non-autopsied cases (35 being fatal):

Normal, 56; signs of active pulmonary tuberculosis (all fatal cases), 3; signs slightly suggestive of tuberculosis, but without diagnosis of tuberculosis, 17; abnormal signs not suggesting tuberculosis, 10.

Condition of the Lungs in 25 Autopsies on Diabetic Cases: Ten cases with pulmonary tuberculosis. Very acute and extensive tuberculosis, 3; mixed chronic and acute, not very extensive tuberculosis, 1; chiefly chronic, slight acute tuberculosis, not very extensive, 1; acute, not extensive, 1. Active, 6 cases. Latent tuberculosis, 1; calcareous (tuberculous?) foci, 1; caseous tuberculous nodule in lung, 1; caseous tuberculous nodule in lung, pleural adhesions, 1. Non-active, 4 cases.

Fifteen cases with no pulmonary tuberculosis. Normal, 2; chronic fibroid pleurisy, 3; congestion, edema, or emphysema, 4; croupous pneumonia, 3; septic infarct, 1; multiple infective infarcts, septic pneumonia, abscesses, 1; abscess and gangrene (adrenal tuberculosis without tuberculosis elsewhere), 1.

Ages of 25 Cases Autopsied in Relation to Tuberculosis: Twenty to thirty years, 5; active pulmonary tuberculosis, 2. Thirty to forty years, 5; active pulmonary tuberculosis, 2. Forty to fifty years, 2; active pulmonary tuberculosis, 0; adrenal tuberculosis, 1. Fifty to sixty years, 7; active pulmonary tuberculosis, 2. Sixty to seventy years, 2; active pulmonary tuberculosis, 0. Seventy to eighty years, 2; active pulmonary tuberculosis, 0. No record, 2; active pulmonary tuberculosis, 0.

Lungs in 4 Autopsies on Colored Persons: Active tuberculosis, 1; Chronic adhesive pleurisy, 1; croupous pneumonia, 1; normal, 1.

CLINICAL AND PATHOLOGICAL DIAGNOSIS IN 7 CASES OF DIABETES, 6 COMPLICATED BY ACTIVE PULMONARY TUBERCULOSIS AND 1 BY ADRENAL TUBERCULOSIS. CASE I.—Male, aged fifty-one years; white. Pulmonary tuberculosis very acute and extensive. Clinical diagnosis: Diabetes mellitus; chronic diffuse nephritis. Pathological diagnosis: Double pleural effusion; chronic adhesive pleurisy; miliary tuberculosis of the lungs and tuberculous bronchopneumonia; miliary tuberculosis of the spleen (?); adhesions of the sigmoid flexure; cardiac (left ventricular) dilatation; fibroid myocarditis; atheroma of the coronary arteries and aorta; chronic mitral and aortic sclerotic valvulitis; chronic interstitial nephritis; renal arteriosclerosis; perilobular hepatic cirrhosis; splenic arteriosclerosis; chronic gastritis; pancreas normal but small.

CASE II.—Male, aged twenty-seven years. Pulmonary tuberculosis very acute and extensive. Clinical diagnosis: Banti's disease; diabetes mellitus; phthisis pulmonalis. Anatomical diagnosis: General tuberculous peritonitis; tuberculous pleuritis, and pleural adhesions; tuberculosis of the lungs (caseous and gelatinous pneumonia with cavity formation); splenomegalia

(Banti's disease); slight chronic interstitial hepatitis (?); slight chronic mitral endocarditis; fatty degeneration of heart and kidneys.

CASE III.—Male, aged twenty-one years; white. Pulmonary tuberculosis very acute and extensive. Clinical diagnosis: Pulmonary tuberculosis; diabetes mellitus. Anatomical diagnosis: Pulmonary tuberculosis; mucoid degeneration of epicardium; slight chronic aortic valvulitis; congested and slightly cirrhotic liver; chronic perisplenitis; congestion of kidneys; moderate cirrhosis of pancreas; mucoid change of peritoneal fat. Histological diagnosis: "Endothelial catarrh" of tuberculous lymph glands (bronchial and mesenteric) with external pigmentation and congestion; miliary tuberculosis of lungs, cavities, and congestion; pleural adhesions and obliterative pleurisy; slight interstitial hepatitis; renal congestion, cloudy swelling, and fibrosis (moderate); slight chronic interstitial pancreatitis; moderate splenic congestion; arteriosclerosis (slight) and hyaline change (slight) in diaphragm.

CASE IV.—Male, aged fifty-eight years, white. Pulmonary tuberculosis, chronic and acute, not extensive. Clinical diagnosis: Tuberculosis of the lungs; diabetes mellitus; arteriosclerosis. Anatomical diagnosis: Caseous ulcerative tuberculosis of the lungs; congestion and edema of lungs; pleural adhesions; slight fibrosis of the kidneys. Histological diagnosis: Caseous tuberculosis, edema, and congestion of the lungs with anthracosis; fibrosis and congestion of the spleen; red atrophy of liver, fatty infiltration, hemosiderin, biliary cirrhosis; chronic interstitial nephritis.

CASE V.—Male, aged thirty-two years; white. Pulmonary tuberculosis chiefly chronic, slightly acute, not very extensive. Clinical diagnosis: Diabetes mellitus. Pathological diagnosis: Obliterative pleurisy of the right side; chronic pulmonary tuberculosis with cavity; chronic valvular endocarditis; chronic interstitial nephritis; atrophy of pancreas.

CASE VI.—Male, aged thirty-three years; colored. Records very incomplete. Pulmonary tuberculosis, acute, but not very extensive. Clinical diagnosis: Diabetes mellitus. Autopsy—Lungs: Both apices showed a large tubercular patch caseating and full of greenish pus, otherwise normal. Heart: Negative. Liver: Normal, infiltrated slightly with fat. The kidneys were decidedly infiltrated with fat and congested.

CASE VII.—Male, aged forty-five years; white. Adrenal tuberculosis (none elsewhere). Clinical diagnosis: Diabetes mellitus; pulmonary tuberculosis. Anatomical diagnosis: Atrophy of the right adrenal; gangrene and abscess of lungs; acute sero-fibrinous pleuritis; fatty degeneration of heart and kidneys; chronic interstitial pancreatitis; arteriosclerosis; acute splenic tumor; multiple superficial erosions of esophagus. Atrophy of the thyroid gland (?). Histological diagnosis: Tuberculosis of adrenals,

slight chronic interstitial pancreatitis. Bacteriological diagnosis: *Streptococcus pyogenes*; *Staphylococcus pyogenes aureus*; *Bacillus coli communis*.

**SUMMARY.** That tuberculosis occurs more frequently in diabetes than in the general population at the same age periods has not been definitely proved by the evidence collected by the writer. However, one is impressed by two facts: (1) The lowered opsonic index to the tubercle bacillus and a number of other bacteria in diabetes; and (2) the large number of cases of diabetes late in the course of the disease developing a very acute, extensive, and rapidly fatal form of pulmonary tuberculosis. Tuberculosis occurs more frequently in diabetes than in some other chronic diseases. The frequency of tuberculosis in diabetes varies with a great variety of different circumstances. In the writer's 25 collected autopsies on diabetic patients, 6 showed active pulmonary tuberculosis varying in acuteness and extent of involvement, and 1 showed adrenal tuberculosis without tuberculosis elsewhere. Out of 355 autopsies collected from the literature since 1882, including also the writer's 25 cases, 138 (38.9 per cent.) revealed pulmonary tuberculosis, mostly in an acute form. In some structures, for example, the bones, the writer could not find a single case of tuberculosis in a diabetic patient.

The frequency of diabetes in cases of tuberculosis is fairly well represented by the table presenting 31,834 cases of pulmonary tuberculosis, of which about  $\frac{1}{3}$  of 1 per cent. had glycosuria, and between  $\frac{1}{6}$  and  $\frac{1}{3}$  of 1 per cent. had diabetes. Five cases of diabetes were found in 937 autopsies on tuberculous patients.

When diabetes and tuberculosis are associated the diabetes can usually be shown to be the primary disease, in a number of cases it is impossible to show which is the primary disease, and in no case that the writer has encountered has the tuberculosis been definitely proved by the evidence furnished to be the primary disease.

When diabetes and tuberculosis are associated in the same patient either disease may show certain modifications in course and symptomatology, but often each disease runs a course apparently independent of the other.

Like the clinical course the autopsy findings may reveal nothing unusual in regard to the tuberculosis, but in a number of cases one meets a tuberculous process that is marked by acuteness, extensiveness of the disease, and tendency to the early development of cavity formation.

From the number of cases that have improved both as to their tuberculosis and their diabetes, one cannot consider the combination of diabetes and tuberculosis as necessarily more hopeless than the diabetes or the tuberculosis alone. The prognosis in many cases depends largely on the treatment.



Space does not allow me to give due thanks and credit to those who are largely responsible for what may be of value in this paper.

To Dr. H. R. M. Landis, Dr. Paul Lewis, Dr. E. J. G. Beardsley, Dr. A. J. Smith, Dr. W. M. L. Coplin, Dr. David Riesman, Dr. I. Kaufman, Dr. C. Y. White, Dr. R. S. McCoombs, Dr. W. B. Bartlett, Dr. R. D. Lyman, and Dr. P. C. Bartlett, I am particularly grateful for information or suggestions. To the physicians of the University, the Pennsylvania, the Episcopal, the Jefferson, the Children's, and the Philadelphia Hospitals I am indebted for the use of records, and to the physicians of a number of sanatoria throughout the United States for important information, and especially to Dr. F. C. Smith and his assistants, of the United States Public Health and Marine-Hospital Service, Fort Stanton, New Mexico, who have furnished me with invaluable data at considerable expenditure of time and labor.

## A FURTHER STUDY OF THE PROGNOSTIC VALUE OF ARNETH'S LEUKOCYTIC BLOOD PICTURE IN PUL- MONARY TUBERCULOSIS, BASED UPON 729 COUNTS IN 475 PATIENTS.<sup>1</sup>

BY PAUL H. RINGER, A.B., M.D.,

ASHEVILLE, N. C.

THREE years ago, in a paper by Dr. C. L. Minor and myself,<sup>2</sup> there were reported the results of the first 100 Arneth counts done by us together with deductions as to their probable prognostic value in cases of pulmonary tuberculosis. At this time it is unnecessary to go into the theory of the causation of this blood picture and its variations. Suffice it to say that the blood picture consists in a differential count of the polymorphonuclear neutrophils with respect to the number of their nuclei. Five classes are recognized according to the number of nuclei in this variety of leukocyte. Arneth claims that in cases with low resisting power there is a preponderance of cells with one or two nuclei, while in cases with good resisting power the percentage of leukocytes with three, four, and five nuclei is increased. Thus in bad cases he obtains what he terms a shifting of the blood picture to the left—"Verschiebung nach Links." This blood picture has been studied and Arneth's conclusions substantiated by many workers, including Arloing and Genty, Bushnell and Treuholtz, Edson, Klebs, Webb

<sup>1</sup> Read before the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 31, 1912.

<sup>2</sup> AMER. JOUR. MED. SCI., May, 1911.

and Williams. The work of Dr. Minor and myself agreed in the main with the results obtained by those mentioned above. We elected to divide our cases according to the clinical symptoms rather than according to the amount of lung involvement, and grouped them into four classes: (1) Good, (2) medium, (3) bad, (4) very bad. Upon going over our counts and making a graphic representation of the results, we found that the one and two nuclei cells were greatest in the classes named "bad" and "very bad," and decreased in the classes named "good" and "medium," while the opposite was true of the cells with three, four, and five nuclei. In a small number of cases—not over 4 or 5—we found together with a good clinical symptom complex a very bad blood picture, and we noted that shortly thereafter the patient took a turn for the worse.

Neither in the counts forming the basis for the paper above referred to, nor in the counts following it, have the polymorpho-nuclear leukocytes been divided into sub-classes (as Arneth was wont to do) based upon the shape of the nuclei—whether indented, S-shaped, crescentic, etc. This has been deemed unimportant. The same arbitrary rules for counting that were advocated in the article written three years ago have been strictly adhered to. These are: (1) Nuclei connected by an isthmus counted as one nucleus. (By "isthmus" is meant a strand of nuclear matter one-third or more of the thickness of the nucleus.) (2) Nuclei connected by a thread counted as two nuclei. (3) Nuclei clearly superimposed counted as two nuclei. (4) Nuclei tangent to one another counted as two nuclei. Thus uniformity of counts done by the same worker was assured.

So much for a very brief review of the former results published by Dr. Minor and myself. Since that time the use of Arneth counts has been continued, and the writer wishes in this article to set forth conclusions arrived at from a total of 729 counts done on 475 patients. In addition to the counts done on tuberculous or supposedly tuberculous patients, the blood of 20 apparently normal individuals has been counted, in order to arrive at a "normal" blood picture.

The average of these 20 counts gives as a normal blood picture the following:

	I	II	III	IV	V	Index
Percentage . . . . .	4	20.5	58.5	15	2	53.75

This average is slightly better than that obtained by Arneth from the average of 15 supposedly normal individuals. His "normal" blood picture reads as follows:

	I	II	III	IV	V	Index
Percentage . . . . .	5	35	41	17	2	60.5

The "index," so-called, is one arbitrarily adopted by Bushnell, and is obtained by adding together the percentages of Classes I and II, and half that of Class III, thus showing what percentage of the cells is to the left in the blood picture. This index has the advantage of showing at a glance whether the blood picture is good or bad, but it has the disadvantage that it tends to relegate into the background the relative proportions of the various classes, and especially that it recognizes no difference between Classes I and II, a difference that is not without importance.

As a result of over 700 counts, the conclusions drawn can be neither as unified nor as satisfactory as those derived three years ago from 100 counts; showing that greater familiarity with a method both enhances its value and indicates its limitations. The writer does not wish to be thought to mean that the Arneth blood picture is to be considered as valueless, misleading, or false. Far from it. The blood picture is of a certain value, it should not be abandoned, and it will in certain apparently favorable cases correctly presage an unfortunate outcome, or *vice versa*. The writer, however, must confess that he cannot place as much weight upon its prognostic value as he did three years back.

First and foremost it must be distinctly understood that the Arneth blood picture can in no way be taken to indicate the amount of lung involvement or the stage of the disease. It is simply and solely an index of the resisting power of the patient. Patients with extensive local lesions—usually of the fibroid type—showing but little activity and having a good general state of nutrition will give a relatively good blood picture; while others with but very slight local lesions, but poor nutritional conditions will give a bad picture. As an example of the first class may be cited the blood picture of a man (J. B. McG.) with fibroid phthisis of fifteen years duration—extensive pulmonary involvement, but good general condition:

	I	II	III	IV	V	Index
Percentage . . . .	12	45	35	7	1	74.5

This is a relatively good blood picture, especially when contrasted with that of the following patient (McD.) having but suspicious signs of a unilateral basal pleurisy, no cough, no bacilli in the very scanty sputum, but in very poor general condition. His blood picture was as follows:

	I	II	III	IV	V	Index
Percentage . . . .	12	42	42	4	0	75

Which is decidedly bad for a patient with such slight evidences of disease.<sup>3</sup>

<sup>3</sup> Since the writing of this paper the patient here referred to reacted violently to 2 mg. of old tuberculin.

Again, improvement in the blood picture or the reverse, indicates a corresponding change in the resisting powers of the patient and that alone. To be sure such changes are usually accompanied by betterment or further extension of physical signs, but there are always patients to be found whose general condition improves markedly while the physical signs remain stationary, just as there are others that begin to go downhill without any detectable change taking place in the local pulmonary condition. It is in such cases that the blood picture is of distinct value. The 3 following cases will illustrate this point:

CASE I.—In a patient running no fever (W. B.), and with slight unilateral apical catarrh, the following relatively bad picture was found:

	I	II	III	IV	V	Index
Percentage . . . . .	20	45	30	5	0	80

One month later the reading was:

	I	II	III	IV	V	Index
Percentage . . . . .	38.5	49.5	10.5	1.5	0	93.5

This was soon followed by an acute exacerbation of his disease which shortly ended fatally.

CASE II.—The patient (Col. B.), a man in excellent condition, showed but the faintest signs of pulmonary involvement—granular or rude breathing at the right apex anteriorly and posteriorly. His blood picture on arrival was:

	I	II	III	IV	V	Index
Percentage . . . . .	3	29	55	12	1	59.5

Seven weeks later, fourteen pounds having been gained, but the physical signs being identically the same, he showed:

	I	II	III	IV	V	Index
Percentage . . . . .	4	20	56	18	2	52

CASE III.—A man (Rev. M. L. B.) of slender build and excessively nervous temperament, pale, anemic, and generally run down, showed at both apices definite breath changes, but no adventitious sounds. His blood picture on arrival was:

	I	II	III	IV	V	Index
Percentage . . . . .	36	48	16	0	0	92

This pointed to an unfavorable termination, despite the slight physical signs. Three months later, having gained much in weight and strength, his lungs showed in addition to the modified breath sounds a few fine crackles at one apex anteriorly and posteriorly. The blood picture at this time, however, showed the following:

	I	II	III	IV	V	Index
Percentage . . . . .	24	42	27	7	0	79.5

A great improvement substantiated by the man's general condition, despite the increase in physical findings.

These 3 cases serve to stress the point that by means of the Arneth blood picture we obtain an index of the general resisting power of the patient, and of that alone.

In mentioning the index used in the blood picture it was stated that it was apt to be misleading by taking the attention away from the percentage of cells in the various classes, and making no differentiation between Classes I and II. The following case well illustrates this point: A patient (F. R. H.) with marked pulmonary and slight laryngeal involvement showed upon arrival the following bad blood picture:

	I	II	III	IV	V	Index
Percentage . . . . .	31	46	20	1	2	87

Two and a half months later, having made great improvement, his picture was as follows:

	I	II	III	IV	V	Index
Percentage . . . . .	15	53	27	5	0	81.5

No very striking difference is seen upon looking at the indices, but it must be noted that the cells in Class I are reduced by over 50 per cent., and the cells in Class IV increased 500 per cent., this being significant despite the loss of cells in Class V.

In the writer's opinion a bad blood picture with the percentage in Class I in excess of that in Class II is far worse than one in which the members of Class II are in the majority.

So far attention has been called to counts tending to prove the value of the blood picture in estimating the resisting power of the patient, and consequently in shaping our prognosis. In all fairness the other side of the question must now be taken up, and cases cited in which the blood picture has been misleading.

It is an undeniable fact that in a small number of cases the blood picture has been at absolute variance with the clinical picture, and the subsequent course of the case has in no way accounted or atoned for the anomalous blood findings. It has been quite impossible to estimate exactly the percentage of cases in which this condition has been found, because of the impracticability of eliminating external (and also internal) agencies that could not be foreseen and that had either a salutary or else a deleterious effect upon the patient. In the writer's opinion about 5 per cent. of the cases show a blood picture totally at variance with the clinical picture, and not borne out by subsequent events. This occurs chiefly in cases with good general symptoms and satisfactory local signs. Two examples will suffice:

CASE I.—A patient (R. S.) came to Asheville in March, 1909, with but slight physical signs and in excellent general condition. However, from the character of the onset of the disease and from the quality of the signs, the trouble was suspected to be of an acute nature. Upon arrival the blood picture was as follows:

	I	II	III	IV	V	Index
Percentage . . . . .	21	55.5	21	2.5	0	87

Two months later, the patient having markedly improved, the picture read:

	I	II	III	IV	V	Index
Percentage . . . . .	23	47.5	29	0.5	0	85

There was practically no change.

Two months later, the general and local condition having shown still further improvement, the picture remained unchanged, to wit:

	I	II	III	IV	V	Index
Percentage . . . . .	20	48	32	0	0	84

The patient has been heard from recently, and is now well and in the best possible condition.

CASE II.—Another patient (R. S. R.) came under observation with but very slight unilateral apical catarrh—no temperature—general condition excellent. The blood picture was distinctly at variance with what would be expected. It read:

	I	II	III	IV	V	Index
Percentage . . . . .	19	52	23	6	0	82.5

The patient has improved, and is in most satisfactory condition, but the last count done reads as follows:

	I	II	III	IV	V	Index
Percentage . . . . .	17	55	24	3	1	84

This count shows practically no change.

It would be wearisome to give more examples. The 2 cases cited amply illustrate the point.

Solis Cohen and Strickler<sup>1</sup> have made a careful study of the Arneth blood picture in cases of pulmonary tuberculosis. Their conclusions are here set forth.

"While the average index showed little change, in most of our individual cases the proportion of cells in the first two classes of Arneth seemed to be increased as the patient improved, and in a number of cases to be decreased as the patient grew worse. Of 27 improving patients whose blood was examined more than

once, an increase in cells with one and two nuclei was observed in 22, and a decrease in 4. Among advancing cases there was an increase in 3, a decrease in 4, and no change in 2. Our figures are opposed to those of all other workers."

Such statements from such reliable authorities deserve serious consideration. It is quite impossible for the writer to explain the discrepancy. It would hardly be likely that the majority of Cohen and Strickler's cases were of the type exemplified by the last two examples cited. The only other way for accounting for the contradictory findings is difference in the method of counting the nuclei, for in certainly 50 per cent. of the cells the nuclei are so placed or so connected that a doubt will arise as to which class the particular cell belongs. Were it possible for all workers in this field to agree upon a common set of rules for the estimation of the number of nuclei, and, furthermore, were it possible for different workers to count each other's smears, the real value of the method would be far better shown.

In a masterful paper on this subject which unfortunately came to the writer's notice but recently, Miller and Reed<sup>5</sup> point out that the nuclei are greatly affected as to their number by the fact of either finger or slide being contaminated with dirt. This is a distinctly valuable point, and also a prolific source of error. It is gratifying to note that such painstaking workers as those just cited, believe that the Arneth blood picture is of real value in prognosis.

In conclusion, the writer would state that in his opinion the Arneth blood picture has a certain definite value in forming a prognosis in pulmonary tuberculosis. It is a corroboratory factor to the general clinical picture, and should never be given much weight in contradiction to the general symptom complex presented by the patient. In a small number of cases it will presage an unfortunate outcome or else will cause us to pause before giving a bad prognosis. In a small number of cases it will remain opposed to all the general indications found in the patient. In the vast majority of cases it will faithfully represent the patient's resisting powers but will not disclose any new features. The Arneth blood picture is to be viewed with conservatism. Few that take it up and study it carefully will ever abandon it entirely, but he that places implicit confidence in its readings and bases his prognostic opinion chiefly thereon, will not infrequently be led into error.

<sup>5</sup> Archives of Internal Medicine, May 15, 1912.

## CHANGES IN THE KIDNEY RESULTING FROM TYING THE URETER.

By J. F. CORBETT, M.D.,

ASSOCIATE PROFESSOR OF EXPERIMENTAL SURGERY, UNIVERSITY OF MINNESOTA.

CLINICIANS agree that atresia of the ureter usually results in hydronephrosis of the corresponding kidney, and that this may remain as a final result or be followed by secondary atrophy. The picture is much the same, whether the condition arises from congenital stenosis of the ureter, or from some sudden blocking of that structure by any cause. The effect on the patient, over and beyond that resulting from the loss of functioning kidney parenchyma, is not definitely and clearly established.

Many of the patients having congenital or long-standing stenosis of the ureter have lived to a ripe old age without having experienced any untoward symptoms. On the other hand, fully as many patients have been driven to seek surgical relief on account of a similar pathological condition.<sup>1</sup>

For a thorough review of this part of the subject, the reader is referred to articles by Allen and Parker,<sup>2</sup> C. N. Dowd,<sup>3</sup> Bottomley,<sup>4</sup> and Eisendrath.<sup>5</sup>

In the series of cases reviewed by Bottomley,<sup>6</sup> there were 3 instances where changes corresponding to some form of nephritis occurred in the non-occluded kidney. In 2 of these cases, 1 reported by Sainsbury,<sup>7</sup> and 1 by Cooper Rose,<sup>8</sup> the probable added factor of a low grade infection must be considered. But in Bostrem's<sup>9</sup> case, where marked changes occurred in the non-occluded kidney, the hydronephrotic fluid did not give any evidence of infection. Further than this, Ord<sup>10</sup> reports a death resulting from a stricture of the ureter, and White<sup>11</sup> a case of coma from a similar condition. From the records of these observers, one is scarcely justified in drawing definite conclusions, except that the results of an atresia of one ureter vary greatly in different individuals.

Turning from the clinical consideration to the experimental laboratory, we find that this subject has received considerable attention. As the conclusions of laboratory workers have not always been identical, I feel justified in reviewing the most important work of the observers.

<sup>1</sup> Louis Frank, New York Med. Jour. 1912, p. 410.

<sup>2</sup> Annals of Surgery, xlii, 265.

<sup>3</sup> Surg., Gyn., and Obstet., xii, 533.

<sup>7</sup> Trans. Path. Soc., London, lxxxvii, 296.

<sup>8</sup> Cited by Bottomley, Annals of Surgery, lii, 624.

<sup>9</sup> Ibid., p. 616.

<sup>10</sup> Trans. Path. Soc., London, xlii, 132.

<sup>11</sup> Trans. Path. Soc., London, xxxviii, 168.

<sup>2</sup> Jour. Exp. Med., ix, 82.

<sup>4</sup> Ibid., lii, 597.

<sup>6</sup> Loc. cit.



Nefedieff<sup>12</sup> found marked changes in remote organs and in the opposite kidney as a result from the ligation of one ureter. Nefedieff assumes that these remote changes were due to a nephrotoxic substance in the blood. No other observer has ever been able to confirm the existence of any such substance, but the important part of Nefedieff's work is that he found changes in the unoperated kidney. That changes such as occur in the non-operated kidney could be due to absorption of nephrotoxic substances from the cells of the normal kidney, is negated by the work of Miss B. Sheldon Amos.<sup>13</sup> Pearce<sup>14</sup> and Aronson<sup>15</sup> also show that the extracts of normal kidneys have no more specific action than cholin derived from any source.

The rabbits in which Miss Amos ligated one ureter, frequently died, and the protocols from these experiments show that there were more or less important changes, such as cast formation or new connective tissue in the unoperated kidneys in about 50 per cent. of the animals. Miss Amos suggests that death occurring at very irregular intervals in these animals was due to some toxic substance elaborated by the operated kidney, and stored in its hydronephrotic sac. Death certainly could not have been due to the loss of function of one kidney, for Sampson<sup>16</sup> and Pearce<sup>17</sup> have established that only one-third of the total kidney substance is necessary to life.

Pearce<sup>18</sup> found the essential lesion of atresia of one ureter to consist of changes in the operated kidney, and only compensatory hypertrophy in the other kidney.

Lindeman,<sup>19</sup> Castaigne and Rathery,<sup>20</sup> Nefedieff,<sup>21</sup> and Sollman, Williams, and Briggs<sup>22</sup> have pictured changes in the tied side. Pearce<sup>23</sup> and Amos<sup>24</sup> confirm these findings.

The length of time necessary to bring about complete destruction of the kidney, as far as its functioning capacities are concerned, has been considered by Sollman, Williams, and Briggs.<sup>25</sup> Inasmuch as the contained hydronephrotic fluid was found not to be urine, but transudate, after four weeks atresia of the ureter, this may be assumed as the minimum time.

This paper will discuss the following conditions: (1) Changes resulting from ligation of the ureter in the kidney on the tied side. (2) The amount of function remaining to the kidney after atresia of the ureter lasting for various periods of time. (3) Lesions remain-

<sup>12</sup> Annales de l'Institut Pasteur, 1901, xv, 17.

<sup>13</sup> Jour. Path. and Bact., x, 265.

<sup>14</sup> Jour. Med. Research, xxi, 313.

<sup>15</sup> Ibid., x, 632.

<sup>16</sup> University of Pennsylvania Med. Bull., 1903, p. 217 (cited by Miss Amos).

<sup>17</sup> Zentralbl. f. allgemein Path. und path. Anat., vi, 184.

<sup>18</sup> Compt. rend. Soc. Biol., 1902, p. 653 (cited by Miss Amos).

<sup>19</sup> Loc. cit.

<sup>20</sup> Loc. cit.

<sup>21</sup> Loc. cit.

<sup>22</sup> Jour. Exp. Med., xi, 430.

<sup>23</sup> Jour. Exp. Med., x, 745.

<sup>24</sup> Jour. Exp. Med., ix, 71.

<sup>25</sup> Loc. cit.

ing in the kidney as a permanent legacy after tying the ureter, and at a subsequent date removing the ligature. (4) Changes in the unoperated kidney.

The ureters were all ligated in the following manner:

Under full ether anesthesia, the abdomen was opened, and after the intestines were packed off, the ureter with a bit of the underlying fascia, was surrounded by a single linen thread. This was tied tight enough to produce atresia without cutting the tissues.

After the operation, the animals were kept in special metabolism cages, and fed a diet of known chemical composition. A record was kept of the animals' condition, and all the urine and feces saved for analysis. In all, twenty-four animals were sacrificed.

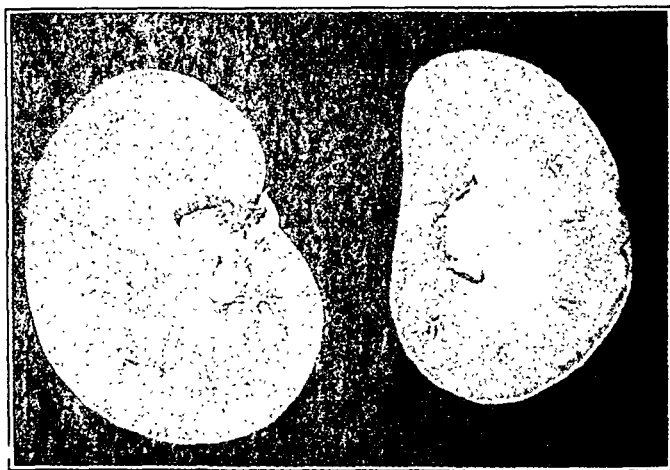


Fig. 1.—Animal experiment 11-56. Left ureter ligated for twenty-four hours. On the left is shown the operated kidney; on the right the control.

#### 1. RESULTS OF ATRESIA OF URETER ON THE OPERATED KIDNEY.

The most striking changes produced by atresia of the ureter are those closely resembling the lesions of nephritis, as the following examples typify. The kidney with a twenty-four-hour stenosis of the ureter, is larger and heavier than on the control side, and presents alternating light and dark areas. The glomeruli are sometimes encircled by a zone of congestion. The convoluted tubules in places are nearly normal, in other places appear to have undergone an extreme degree of degeneration, so that in place of normal epithelial cells lining these structures, we have left only a mass of granular detritus. The tubules of the kidney generally are dilated, and this dilatation is more marked as we approach the pelvic outlets of the collecting tubules. The kidney of which the ureter had been ligated for six days, presents a still more striking appearance as it is very pale and edematous, with increase of size and weight. The pelvis shows marked hydronephrosis. There is general deformity of the tubules, extensive degenerative changes

in the convoluted tubules and the beginning formation of new connective tissue. In the collecting tubules masses of detached epithelium are frequently seen. At the end of twenty-six days, a ligated kidney presents an extreme picture of hydronephrosis, so that it is actually converted into a very thick-walled cyst. The kidney substance is white and is cut with difficulty. On the surface are retracted areas corresponding to bands of connective tissue seen on the cut surface. Under the microscope the cortex consists of a mass of connective-tissue cells, round cells, dilated and deformed tubules, nearly normal glomeruli, and all stages of cast formation.

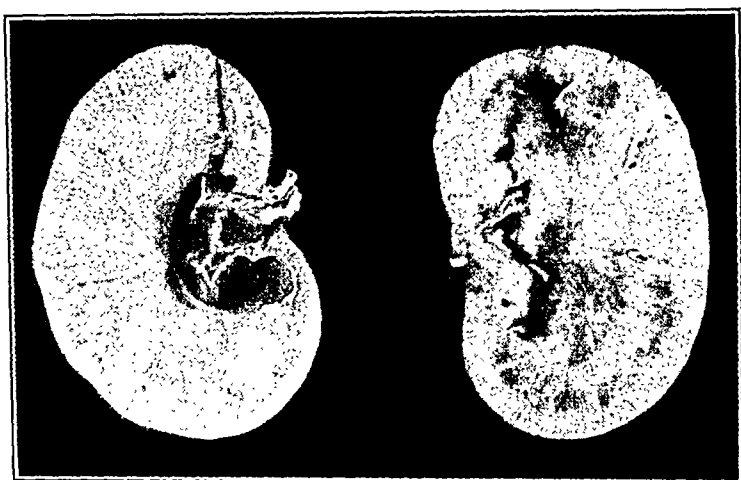


FIG. 2.—Animal experiment 11-61. Left ureter ligated for twenty-six days. On the left is shown the operated kidney; on the right the control.

These pictures are the most striking examples encountered in a series of four animals for each period of time. In some of the animal experiments, the changes given above appear to so slight a degree as to seem almost negligible. In these cases deformity of the tubules and fatty metamorphoses are marked. In the twenty-four-day series, the extent of destruction of the parenchyma seems to be about the same whether the picture is that of fatty change or that of nephritis. In a very few instances the damage is erratic in that it is localized.

2. The histological findings in this series indicate very extensive destruction of the kidney substance on the operated side, as the result of tying one ureter. To determine whether enough of the kidney parenchyma was destroyed by these processes to ablate the secretory function of the kidney, the urine was collected from kidneys whose ureters had been so occluded for various periods of time, measured, and analyzed.<sup>26</sup> In Table I, under Animal Experiment, 11-58, the nitrogen content shows that the kidney

<sup>26</sup> *Annals of Surgery*, xliii, 725.

the ureter of which had been ligated for twenty-four hours was for a time capable only of excreting urine in a very irregular manner. This kidney in time resumed its full function. The amount of chloride excreted also varied from day to day, but showed less general departure from the normal than the nitrogen.

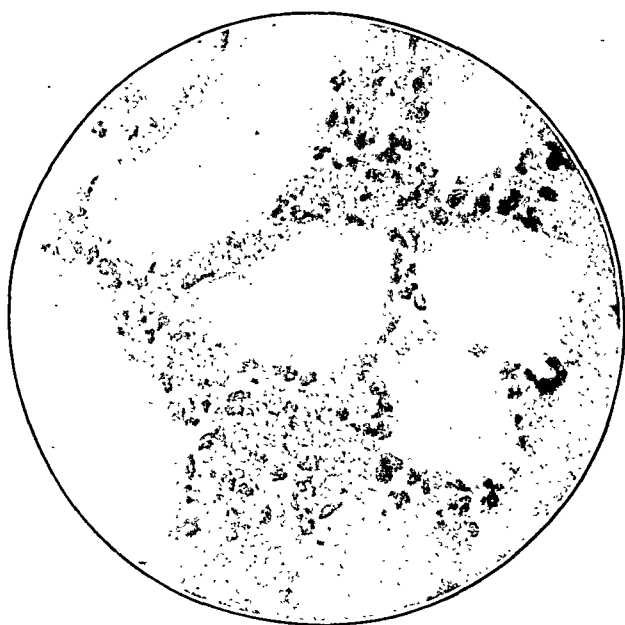


FIG. 3.—Animal experiment 11-56. Left ureter ligated for twenty-four hours. Shows necrotic epithelium of convoluted tubules surrounded by zone of active inflammation.

TABLE I.—Animal Experiment 11-58.

No of sample.	Date.	Quantity c.c.	Nitrogen per c.c.	Total nitrogen in 24 hours.	Albumin.
...	October 18	0	0	0	
157	October 19	170 <sup>25</sup>	0.01084	1.842	+
...	October 20	0	0	0	
164	October 21	85	0.01554	1.320	+
...	October 22	0	0	0	
169	October 23	150	0.008405	1.260	+
...	October 24	21	0	0	
179	October 25	75	0.006818	0.511	
...	October 26	0	0	0	
189	October 31	65	0.01322	0.859	+
..	November 1	0	0	0	
196	November 2	95	0.012049	1.144	+
201	November 3	80	0.008728	0.698	
207	November 4	90	0.008817	0.783	
212	November 8	70	0.009796	0.685	+

Average nitrogen per day before operation, = 0.539. Average nitrogen per day after removing ligature, both kidneys secreting, = 0.637. Nitrogen from ligated kidney after removing right kidney as above.

Left ureter ligated October 9; ligature removed October 10; right kidney removed October 18.

<sup>25</sup> The full capacity of the bladder was 45 c.c. at autopsy.

TABLE II.—Animal Experiment 11-62.

Average nitrogen per day before operation, = 0.396. Average nitrogen per day from ligated kidney, = 0.350. Left ureter ligated October 11; ligature removed October 17; right kidney removed October 24.

The kidney that had been ligated for six days (see Table II, Animal Experiment, 11-62), after a reasonable length of time, was capable of excreting urine containing an amount of nitrogen compatible with nitrogenous equilibrium, while the kidney that had been ligated for twenty-four days (see Table III, Animal Experiment, 11-64), at first was able to excrete almost nothing at all. Subsequently, it partially regained its functioning capacity and at a later date almost entirely lost that capacity.

TABLE III.—Animal Experiment 11-64.

No. of sample.	Date.	Quantity c.c.	Nitrogen per c.c.	Total nitrogen in 24 hours.	Albumin.
249	November 30	15	0.00788	0.118	
250	December 1	55	0.00606	0.333	
251	December 2	87	0.00523	0.455	+
252	December 4	345	0.00066	0.227	
253	December 6	300	0.00077	0.231	

Average nitrogen per day before operation, = 0.680. Average nitrogen per day from right kidney, = 0.490. Average nitrogen per day from ligated kidney as above. Average from December 15 to December 26 = 0.303. Weight constant.

Left ureter ligated November 6; ligature removed November 29; right kidney removed November 29.

The urinalyses in general confirm the histological pictures.

3. Permanent lesions left after removal of the ligature. In the first example the ureter was ligated for twenty-four hours, the ligature then removed, and after eight days the unoperated kidney was removed. The animal was killed at the expiration of forty-four days after the first experiment. The ligatured kidney is larger than normal. Some slight gross evidence of connective tissue can be seen. Aside from a few hemorrhagic spots in the cortex and the slightly thickened medulla, nothing else is of interest. Under the microscope scattered areas of connective tissue and round-cell infiltration are occasionally encountered. The animal whose ureter had been ligated for six days, ligature then removed, and after another six days the unoperated kidney removed, was killed at the end of seventy-four days after the first operation. The following conditions were noted at autopsy: The operated kidney is large and there remains some evidence of former hydro-nephrosis. The tubules are still somewhat deformed, and the epithelium lining these tubules has an abnormal appearance. Scattered areas of connective tissue also occur. The permanent results of twenty-four days' ligation of the ureter is shown in Animal Experiment, 11-86. In this the ureter was tied for twenty-four days, when the ligature was removed and a nephrectomy done

at the same time on the opposite kidney. The animal was killed after thirty-seven days more. "The operated kidney is pale and shows areas of scar tissue on the cut surface, and retraction on the

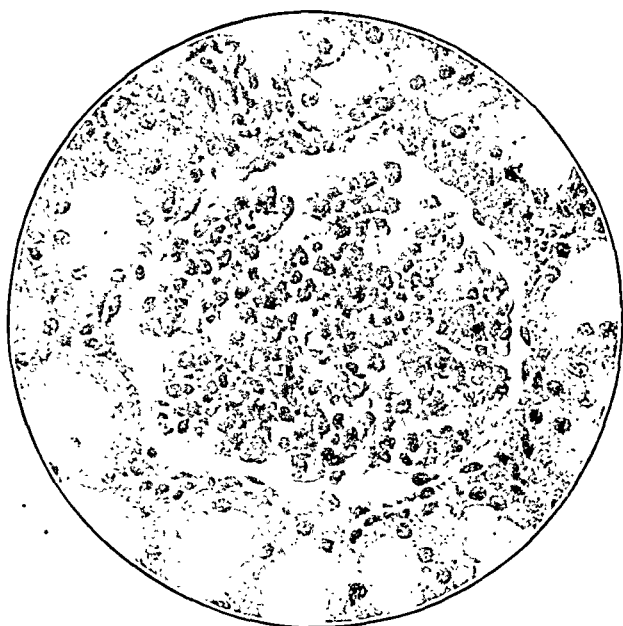


FIG. 4.—Animal experiment 11-56. Left ureter ligated for twenty-four hours. Shows glomerulus compressed; capsule surrounded by zone of congestion; dilated convoluted tubules with slightly compressed epithelium.

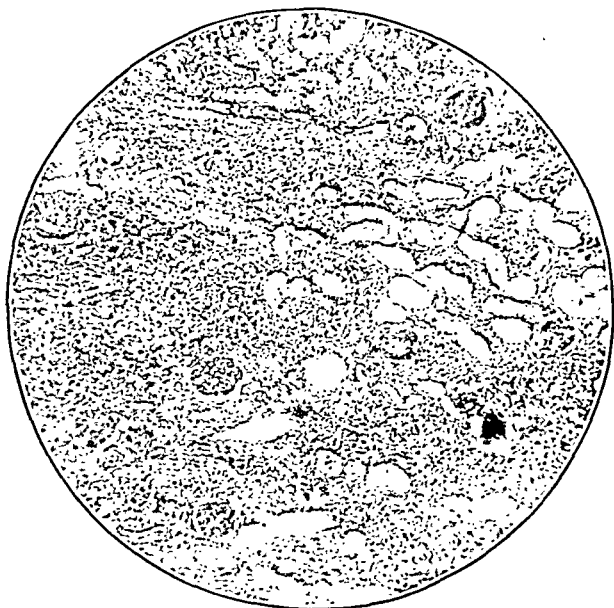


FIG. 5.—Animal experiment 11-61. Left ureter ligated for twenty-six days. Operated kidney; shows large areas of scar tissue incorporating remains of glomeruli and convoluted tubules.

outer surface. There are some remains of old hydronephrosis. There are some wedges of connective tissue incorporating remains of convoluted tubules. The urine from this animal contains casts and albumin."

In Animal Experiment, 11-64, the ureter was ligated for twenty-three days, when the ligature was removed together with the unoperated kidney. The animal was killed at the end of fifty-five days. The operated kidney in this animal presented the same areas of scar tissue and round-celled infiltration incorporating epithelial remains.



FIG. 6.—Animal experiment 11-61. Left ureter ligated for twenty-six days. Shows convoluted tubule with altered epithelium and remains of cast; also new connective tissue and round cells.

4. Changes in the unoperated kidney. It is with considerable hesitation that the author undertakes to describe the changes aside from those of compensatory hypertrophy in the unoperated kidney. These changes occur sometimes not at all and always at very irregular intervals. As has been predicated in the beginning of this paper, various authors have considered that the changes in the unoperated side were due to substances absorbed from the pelvis of the operated side, and that these substances are somewhat nephrotoxic. For this reason I have taken the contents of these hydronephrotic kidneys obtained after various periods of time, and injected them into normal rabbits. No ill effects in these animals was noted except that following the injection of the fluid there seemed to be a decrease in the amount of nitrogen excreted. At autopsy at the end of twenty-four hours, the kidneys of 2 of

these animals presented some slight pictures of congestion. In one instance the unoperated kidney presented only evidence of compensatory hypertrophy, and the fluid from the operated side had no nephrotoxic properties whatever.

If we exclude such changes as slight dilatation of the tubules and fragmentation of the protoplasm of the cells due to artefacts, no important lesions occurred in the non-operated side of the one day or the six day rabbits. In 2 of the animals in which one ureter had been ligated for a period of twenty-three days, there occurred more or less change in the unoperated kidney. We can absolutely, I believe, exclude the question of changes antedating the operation, by the fact that all of these rabbits had very careful quantitative urine analyses made for a period of several days before operation. Those presenting any anomalies in the urine were rejected for operation.

The changes in the unoperated kidneys of the twenty-four day rabbits did not seem to bear any definite relation to each other, and varied from the occurrence of a few hyaline and epithelial casts to a condition of round-cell infiltration, and even scar tissue production. In cases where nitrogen determinations were made of the urine from the unoperated side, it was frequently found that there was an increase of nitrogen and usually some albumin (see Table IV, Animal Experiment, 11-61). This oftentimes persisted for a longer period of time than could any immediate effect of the anesthetic have lasted. In 2 animals only compensatory hypertrophy occurred in the control kidney.

TABLE IV.—Animal Experiment 11-61.

Average nitrogen per day before operation, = 0.566. From October 12 to October 26 variable. Average nitrogen per day from non-ligated kidney, = 0.693. Ureter ligated October 11. Animal killed November 6.

**CONCLUSIONS.** At the commencement of this work, the author hoped to be able to tell in a single word whether or not it would always be necessary to remove a kidney having an atresia of the ureter from any cause. He soon found that the answer must be as ambiguous as that of the Delphic oracle, for the results of atresia of the ureter do not always seem to be the same. However, these facts remain: There almost always results severe destruction of the kidney after prolonged obstruction. To save anywhere near the full functional capacity of the kidney, the obstruction must be removed not later than six to ten days. Beyond twenty-four days the removal of the kidney seems justifiable on the following grounds:

1. There remains but little functioning kidney.
2. Hydronephrosis is a common result of atresia of the ureter. The existence of hydronephrosis is always a potential danger.



These sacs frequently mechanically cause disturbance and if one is infected it may become a veritable Vesuvius.

3. In some cases there occur changes in the unoperated kidney and we are led to assume that these changes result from the presence of the no longer functioning kidney. Whether infection of the hydronephrotic fluid by low grade bacteria is the cause of these unoperated kidney changes, does not alter the conclusion.

#### ADDITIONAL REFERENCES.

- P. A. Lewis. *Jour. Med. Research*, xvii, 291.  
 E. H. Fenwick. *Trans. Path. Soc., London*, xxxvii, 300.  
 T. G. Brodie. *Jour. Phy.*, xxxiv, 225.  
 G. E. Brewer. *Surg., Gyn., and Obstet.*, vi, 699.

## CLINICAL MANIFESTATIONS OF ILLUMINATING GAS POISONING.<sup>1</sup>

By ROBERT S. McCOMBS, M.D.,

ASSOCIATE IN MEDICINE, PHILADELPHIA POLYCLINIC AND ASSISTANT PHYSICIAN TO THE  
 CHILDREN'S HOSPITAL, PHILADELPHIA.

DURING the last ten years I have had the opportunity to observe 1000 cases of illuminating gas poisoning in several cities through connection with the medical staffs of several of the large gas companies of the United States. Many of the cases observed have been repeatedly examined, some over a period as long as two years. The employees of the companies in the large gas generating plants, and members of the street gangs, who come more in contact with illuminating gas than others, have been under direct observation throughout these years. During this time some of the men have been overcome fifteen or twenty times, and this has given the opportunity to study the so-called cases of chronic gas poisoning.

It is obviously impossible in the limits of this paper to note the full classification of symptoms and actual statistics of my studies. I will, however, give a complete summary of the results based upon studies of the records and personal observations.

Physiological chemistry: The toxic action of illuminating gas has been fully described by such authors as Sellman,<sup>2</sup> Haldane,<sup>3</sup> Edsall,<sup>4</sup> Crile and Lenhart.<sup>5</sup> To summarize:

In illuminating gas, as furnished by the better companies, the carbon monoxid present is the poisonous principle, the other constituents used to increase the candle power are non-toxic. Carbon

<sup>1</sup> Read by invitation, before the College of Physicians of Philadelphia, May 1, 1912.

<sup>2</sup> Pharmacology.

<sup>4</sup> Osler's Modern Medicine, vol. vii.

<sup>3</sup> Hale White's Pharmacology.

<sup>5</sup> AMER. JOUR. MED. SCI., October, 1907.

monoxid has an affinity for hemoglobin three hundred times greater than oxygen; it excludes the oxygen; the resulting compound is not perfectly stable so that when oxygen is present in very great excess the carbon monoxid hemoglobin will be decomposed and oxyhemoglobin formed. While oxygen cannot directly displace the carbon monoxid, it has been established that dissociation of the carbon monoxid hemoglobin occurs under these circumstances, and that the carbon monoxid is expired as such, no noteworthy amount being oxidized into carbon dioxid. At death as much as 60 to 80 per cent. of the hemoglobin in the circulation will be in combination with carbon monoxid. The resultant symptoms are due principally to a diminution of the supply of oxygen to the tissues of the body. There is also a direct toxic action in the human being. At first there is a stimulation of the central nervous system, followed by paralysis, the order being brain, spinal cord, and medulla. There have been several instances in which plants have been destroyed by gas.

For purposes of convenience the various symptoms of illuminating gas poisoning have been divided into three stages, this is my own classification, conceived with the idea of giving employees definite divisions for the application of first aid methods.

**SYMPTOMS.** The first stage continues until the patient loses consciousness. During this period the following symptoms will develop: Cerebral excitement and dilatation of the cutaneous vessels, occasionally cyanosis will be noted if the poisoning is very acute, the venous blood being practically free from carbon monoxid; dizziness; headache; pains in the extremities; muscular twitchings slow pulse from stimulation of the pneumogastric; rise in blood pressure from stimulation of the vasomotors; there is a feeling of constriction of the chest, rarely actual dyspnea; wide dilatation of the pupil; nausea and vomiting. Late in this stage there is a feeling of general weakness, faintness, languor, and at times, stupor. Some times there is delirium. The temperature is normal or slightly elevated.

The second stage begins with syncope and ends with apnea. The patient is unconscious but breathing, the respirations are rapid and stertorous with a corresponding increase in the pulse; the blood pressure falls; the temperature is elevated, at times reaching degrees of hyperpyrexia; there may be loss of sphincter control and of some of the reflexes, although these are not constant. At times there are general tetaniform convulsions. Some cases show only a profound state of coma without the above-mentioned symptoms, one case I saw in consultation had persisted for nine days, this man had not been properly treated according to our present knowledge. Toward the end of the second stage there is general muscular rigidity and a weak rapid pulse at times as high as two hundred; the jaws may be stiff and the tongue swollen; the peculiar cherry-red markings, so characteristic after death,

may make their appearance on the skin of the neck, trunk, and thighs. The spectroscope will show the presence of carbon monoxid in the blood. The respirations gradually become weaker until there is apnea.

In the third stage the patient is comatose and respirations have ceased. A very rapid, weak, intermittent heart action is all that indicates the presence of life. All symptoms of asphyxiation are present except cyanosis, which is absent unless poisoning has been very sudden. In the slower, gradual poisoning we may find the cherry-red markings of the skin. The presence of carbon monoxid in the blood may be determined by the spectroscope. The muscular rigidity before mentioned may be present.

**DEATH.** If the skin surface is not discolored at death, within an hour or two it will become deeply marked especially in the dependent parts with cherry-red areas. Likewise, the toes will become fully extended and the hands assume the tetany position. This extension of the toes and fingers seems to appear after death earlier in children than in adults. At postmortem examination the organs are deeply injected, especially the spleen, there may be scattered small hemorrhages and at times cerebral changes, particularly areas of softening in the lenticular nucleus, symmetrical in many cases. (Spiller.) The blood is pink in dilute solutions and shows the presence of carbon monoxid by the spectroscope.

The test suggested by Hoppe-Seyler—namely, that blood containing carbon monoxid treated with double its volume of a solution of sodium hydrate yields a beautiful red color when spread on a porcelain plate, while ordinary blood under the same conditions is changed into a dirty brownish mass, which exhibits a trace of green—has not given satisfactory results.

A fairly accurate test is the action of the blood when it comes in contact with the atmosphere, if it immediately turns scarlet carbon monoxid is probably not present to any great extent as its presence retards the formation of oxyhemoglobin. The spectroscope, however, is the most accurate method.

The length of time necessary for a person to pass from one stage into the other is uncertain, two factors determine this, (1) the amount of gas inhaled, and (2) the personal idiosyncrasy. Under ordinary conditions a man can breathe a high degree of carbon monoxid for two minutes without symptoms, some of the men can stand it for five minutes. There are some exceptions to this rule, I have seen men pass almost immediately from the first into the third stage after inhaling a small quantity of gas. One can never be sure that an individual who is apparently only slightly affected will not pass into the second or third stage very suddenly and without premonitory symptoms, this is not common, but a person suffering from the effects of gas should be constantly watched.

Another phase is shown by the following: A young colored girl

who had been exposed to a mild degree of carbon monoxid, and apparently had no symptoms whatsoever, at the end of twenty-four hours developed stupor, severe pains in her extremities, and a temperature of 102° F. In the meantime she had not been within several blocks of the leaking gas. These cases are the exception not the rule. If a patient is breathing well when rescued the test for carbon monoxid is hard to get after three hours and the danger of direct death from the immediate poisoning is over in about one hour. When respirations are shallow the time is lengthened.

**SEQUELS.** Symptoms that persist after the blood is free of carbon monoxid are referable principally to the nervous system. They include neuralgia, nervousness, insomnia, pain, intention tremors, loss of sexual power, loss of continuity of thought, delirium, confusional insanity, transient hemiplegia, glycosuria, and prolonged fever. There have been cases of bronchopneumonia. I have not seen any cases of multiple sclerosis, ocular changes, nystagmus, paralysis of the recti, protrusion of the eyeball, hemianopsia, nor gangrene which have been reported. All of the sequels mentioned have eventually cleared up entirely within a period of six months or less. They constitute less than 2 per cent. of all the cases and are almost entirely confined to advanced second stage cases and third stage cases. Any method which tends to shorten the period during which the blood is impaired will tend to prevent the late symptoms due to tissue injury. There have been individuals poisoned by illuminating gas who have been suffering at the time from chronic organic involvements of almost every description, many pregnant women are included in these statistics, also patients with tuberculosis and several who were in the midst of typhoid fever. None suffered any permanent bad effects and no miscarriages have occurred; the children when born have been normal. Sequels are more likely to occur in those of advanced years.

**PROPHYLAXIS.** It is not the purpose of this paper to belittle the poisonous nature of carbon monoxid. The fact remains, however, that deaths result in nearly all cases from preventable causes.

It should be noted in comparing this statement with various reports of accidental deaths from carbon monoxid poisoning, which amounted to 624 in twenty-three years in the State of Massachusetts, as reported by Sedgwick and Schneider, that the cases may be divided very sharply into two classes of accidental poisoning.

1. Those in which the accident consists in a direct break in a pipe in a room; failure to close the gas jet (the usual method); or by other accidental causes of a similar nature, all of which produce contamination of the atmosphere with a high degree of carbon monoxid in a short time.

2. Accidental cases due to street leaks; due to cracking of the

mains by frost; the unequal contraction of frozen ground will break the pipes. At times the escaping gas cannot filter through the superimposed earth, but works its way through water and rat holes or along pipes into the cellars. The odor of gas is always noticeable. In Philadelphia there has been only one instance where death has resulted from the second class of cases and this was preventable.

Suicidal cases make up approximately one-half of all the fatalities here and in Massachusetts.

The majority of deaths were preventable if the individuals had slept with open windows, had paid attention to leaking gas and had reported it immediately, and of course, if they had properly closed the gas stop.

**TREATMENT.** The essential of treatment consists in the inhalation of oxygen, under pressure whenever possible. The object of all plans of treatment is to supply oxygen in sufficient quantities to displace the carbon monoxid in combination with the hemoglobin.

Oxygen inhalations are indicated in all stages.

In first stage cases fresh air combined with mild stimulation, such as aromatic spirits of ammonia, should be administered. In this stage the nausea, vomiting, and headache are the most troublesome symptoms. The greater part of the gastric symptoms will be relieved by some effervescing salt, the patients feeling much better after eructating or vomiting. It is due to this relief from nausea and gastric distention that a peculiar remedy for gas poisoning obtained its reputation as an antidote among men working in gas; it is an effervescing birch beer, called "Weiss Beer." Effervescing phosphate of soda has been substituted. There is no true antidote for gas poisoning other than oxygen. The headache usually persists for twenty-four or forty-eight hours and may be relieved by any of the drugs used for this condition. Violent exertion is to be avoided, as collapse is a danger; men who have become aggressively delirious have collapsed.

Second stage. The patient is unconscious but breathing. It may be necessary if the respirations are not stertorous to assist the respiratory action. The Howard method (compression of the lower part of the chest in rhythm with expiration) has been found efficient. Oxygen must be administered preferably under pressure. Haldane placed animals (mice) in oxygen under a pressure of two atmospheres, so that simple solution of oxygen in the blood serum was obtained sufficient to support life independently of the hemoglobin. Enough carbon monoxid was present to completely saturate their hemoglobin. Under these conditions the animals remained normal as to symptoms, showing that the carbon monoxid had no direct toxic action. When the pressure was removed and the mice put out in the air they died with symptoms of asphyxia.

Various mechanical devices for administering artificial respiration and supplying oxygen have been tried but until lately all were unsatisfactory. At present the "pulmotor"<sup>6</sup> is being used. This machine automatically adjusts itself to the individual capacity of the lungs, without danger of rupture, and maintains a mixture of oxygen and air (60 per cent. oxygen) under a constant pressure of five atmospheres. It maintains artificial respiration perfectly. Reports from all over the country relative to its efficiency have been received. Whenever possible it should be used. Undoubtedly the prompt suction by the "pulmotor," of the carbon monoxid present in the residual air and that which is being constantly eliminated from the blood, materially aids resuscitation.

Medicinally the patient should be freely given hypodermics of stimulants such as camphor, caffeine, digitalis, and strychnine. Heat should be applied when indicated and as there are several cases in which the persons have collapsed when taken out into cold air, it is always better to start treatment in a warm room. A very important adjunct to this plan of treatment is the massaging of the muscles after aerating the lungs, the increase in the hemoglobin in the general circulation accomplished by it often promptly restores the normal oxygen balance.

The above methods are usually followed by prompt recovery. If they are not successful, venesection with the introduction of normal salt solution should be employed. Two cases have come under my personal observation at the Philadelphia Polyclinic Hospital in which this method was followed by rapid and complete recovery, although there was some mental confusion in both cases for some time. Favorable reports of cases treated by this method are made by Jersey, Wilkie, Schruher, and von Gordon, 8 in all, and including the 2 mentioned above making 10. Crile and Lenhart<sup>7</sup> report 5 deaths at the Cook County Hospital, Chicago in which this method was employed. I believe it should be employed when the patients are in fairly good condition when rescued, that is, a fair pulse, stertorous respirations, unconscious, and with no immediate signs of collapse. However, the "pulmotor" has made its necessity less frequent. Venesection and transfusion of defibrinated blood was practised by some clinicians in the seventies, those for and against this method were about equally divided. Should the "pulmotor" fail, the best method is the direct transfusion of blood as practised by Crile and his followers. His experiments, reported in the AMER. JOUR. MED. SCI., led him to conclude that blood transfusion seems to be of greater therapeutic worth than the other measures considered. It has been used in 2 cases in Philadelphia, both of which made a prompt recovery after other

<sup>6</sup> The pulmotor is manufactured by the Draeger Oxygen Apparatus Co., Pittsburg, Pa.

<sup>7</sup> Loc. cit.

methods had failed. The introduction of fresh hemoglobin which will combine with oxygen and which will not be contaminated by the carbon monoxid already held in a combination with the patient's hemoglobin is a sure way of restoring the normal oxygen balance. Transfusion should be done immediately if the patient is in the advanced second or in the third stage and fails to respond to the ordinary treatment. The only objection to this plan of treatment, according to Dorrence, is the fact that about 25 per cent. of transfusion operations are failures unless undertaken by skilled surgeons.

Third stage. The patient is not breathing and is unconscious. Artificial respiration, oxygen, stimulation and heat are imperative. Transfusion is indicated. The Schafer or "prone pressure," method of artificial respiration is the best to use. The "pulmotor" has maintained artificial respiration in this stage.

Artificial respiration has been maintained for six hours with subsequent recovery of the patient.

PROGNOSIS. If the above methods of treatment are carried out and the patient is not dead when discovered practically all cases should recover in forty-eight to seventy-two hours from the immediate effects of the gas, no matter how concentrated the carbon monoxid causing the poisoning. The great difficulty in treatment has been the failure of both laity and physicians to realize that inhalation of oxygen under pressure combined with venesection or blood transfusion in severe poisoning will save practically all the cases.

Of 39 cases reported by Edsall<sup>8</sup> occurring at the Episcopal Hospital in Philadelphia, mostly suicidal in intention, 34 fully recovered and most of the fatalities were due to sequels.

The possibility of sequels developing sometime after the poisoning must be borne in mind, but all such cases in my experience have cleared up within six months.

Gilman Thompson<sup>9</sup> considers it a bad sign if leukocytosis, which he says is usually present, be of a high degree.

CHRONIC GAS POISONING. Examinations of the blood of men who are constantly in contact with carbon monoxid, and of some who have been repeatedly poisoned, have been made. The average count shows a polycythemia. This is in accord with the report of the investigating committee authorized by the Illinois Legislature and published in the *Journal of the American Medical Association*, also with the 2 cases reported by Reinhold.<sup>10</sup>

I could not find any muscular weakness in the men examined. Some of them had been employed in this line of work for twenty years and are now among the strongest and healthiest individuals I know. As a rule, they pay no more attention to first-stage gas

<sup>8</sup> Loc. cit.

<sup>10</sup> Ibid.

<sup>9</sup> Cited by Edsall.

poisoning than the average person would to a headache. The estimation of muscular weakness by comparison with men in other occupations is difficult to obtain and is unreliable at best.

I have seen no accumulative action of carbon monoxid unless the polycythemia may be an evidence of it. Reported symptoms such as irregularity of the heart, slow pulse, anemia, lack of concentration, poor memory, cardiac dilatation, splenic enlargement, and pleural effusions have not been observed in the laboring class I have had under observation.<sup>11</sup>

Evidently the increase in the red blood corpuscles, the polycythemia, is to compensate for the presence of small quantities of carbon monoxid so that the normal supply of oxygen to the tissues can be maintained.

<sup>11</sup> I think illuminating gas is blamed for a large number of cases of serious chronic poisoning which are due to defective heating apparatus and to broken furnace pots.



## REVIEWS

---

**SURGICAL OPERATIONS. A HAND-BOOK FOR STUDENTS AND PRACTITIONERS.** By PROFESSOR FRIEDRICH PELS-LEUSDEN, Chief Surgeon to the University Surgical Clinic and Chief of the University Surgical Polyclinic in the Royal Charity Hospital of Berlin. Only authorized English translation; by FAXTON E. GARDNER, M.D., New York. Pp. 726; 668 illustrations. New York: Rebman Company.

PROFESSOR PELS-LEUSDEN has taught operative surgery for many years, and, as he states in his preface, the present book is born from a desire to link together what he has long taught in practical courses and theoretical lectures. Like many writers he addresses his book to students and general practitioners, and modestly adds that he will feel gratified if the *specialist*, by which term it is presumed he means the accomplished surgeon, shall find therein anything useful.

The operations of surgery are discussed regionally: Extremities, head, neck, thorax, abdomen, and genito-urinary organs. Operations on the female genitalia are not included. But before this regional portion of the work there are important chapters on antiseptics and asepsis, anesthesia, division and reunion of the different tissues, and surgery of the bloodvessels.

There is much in this volume that is unfamiliar to the majority of surgeons not thoroughly informed of current German teaching; but surgeons of other nationalities, especially American surgeons, will look in vain for many procedures that to them are operations of routine. An American operation that is twenty, or at the least, ten years old, finds its place in this volume and is described as a novelty. There is nothing described so modern as endo-aneurysmorrhaphy. The V-shaped excision of the lower lip is described as if no better plan could be desired. There is no mention of Dowd's transverse cervical incisions for extirpation of lymph nodes. The muscle-splitting incision for exposure of the appendix is described, but it is not distinguished by McBurney's name; while Lennander's name is given to the incision previously described by Battle, by Kammerer, and by Jalaguier, none of them, surgeons practising in Germany. A "complicated" method of operation for the radical cure of umbilical hernia is quoted from Graser, as if the writer

himself had no familiarity with it; and in parenthesis he mentions that Graser says the method of suture had been used before in similar cases by Girard, Mayo, Baracz, and others. This is the only description of the "Mayo" operation, which in this country is thought both useful and sufficiently simple of execution. There is no mention of Ruggi's inguinal method in operations for femoral hernia.

On the other hand, as stated above, there is a great deal that might well be adopted in this country, as well probably as in Great Britain. Especially worthy of note is the extent to which local anesthesia is employed by the German surgeons. Though it is certain that operations on phlegmatic Germans may be more easily conducted without the influence of a general anesthetic than those on more sensitive individuals, it is equally true that many more operations in this country could be successfully performed under local anesthesia than the average surgeon here realizes. The operation must be conducted more slowly, and the manipulations must be immeasurably more gentle; but in certain classes of cases the results are worth all the trouble that the method entails; and nowhere can the operator learn the method better than from this book.

Another instance of progressiveness in German surgery is the apparent freedom with which the brain is explored. Nothing sounds more simple than to spray the scalp at the desired point with ethyl chloride; then to bore through the skull with a gimlet driven by electricity or by hand; and finally, to insert a long hypodermic needle through this hole and explore the brain by creating negative pressure in the barrel of the syringe. The only question that comes to the mind of a practical American surgeon after reading the description will be "what will I learn even if I get some fluid or particles of brain substance?"

So, under "Trephining," Pels-Leusden says "in former times we used the so-called trephine." Nothing so old-fashioned is recommended today; only bits and braces and Gigli saws and Dahlgren forceps are advised, apparently forgetting that bits and braces, in the form of the old "trepan" long preceded the "so-called trephine." Cushing's subtemporal decompression is mentioned, doubtless because his early brain surgery was done with Kocher; if it had been purely American bred next to nothing would be known of it in Germany. Thus there is no mention of the Spiller-Frazier operation for trigeminal neuralgia.

The illustrations are not beautiful, but show what the author wishes. Almost all are diagrams. The student will profit by this as well as by the attention paid to the details of the operations described, and to the preparation and after-care of the patient. The reasons for the various recommendations are given, and thus the author's advice is more easily remembered. The important

place given to applied anatomy in the descriptions of operations is characteristic of a careful and successful operator.

The translator has done his task well, preserving the German idiom, and using an abundant number of Anglo-Saxon words, which render the text altogether delightful and refreshing.

Comparisons are odious; but this volume naturally lends itself to comparison with Kocher's Operative Surgery, which through the excellent translation of Mr. Stiles is more familiar to English reading surgeons than any other work of the kind by a foreign author. The work of Prof. Pels-Leusden of course does not enjoy the great prestige which attaches to a text-book from the pen of the Prophet of Berne; he is content to take operative procedures as he finds them, and does not convert others' methods into original operations by the mere process of absorption. There is an old saying whose truth always seems challenged when a text-book by Kocher is consulted. This is the saying that the originality of most men consists in their ignorance of the work of others. Kocher cannot be charged with ignorance of anything in surgery; yet almost all his operations are described as original with himself. This is not the case with Pels-Leusden. The two text-books cover about the same ground, though Kocher's has grown to an immense size in its later editions. Pels-Leusden will do well if he can preserve the present athletic figure of this child of his brain when it has reached middle life. *Μέγα βιβλίον μέγα χαλόν.*

A. P. C. A.

---

SERUM DIAGNOSIS OF SYPHILIS. By HIDEYO NOGUCHI, M.D., M.Sc., Associate Member of the Rockefeller Institute for Medical Research, New York. Second edition; pp. 238; 14 illustrations. Philadelphia and London: J. B. Lippincott Company.

THIS book was the first English effort to put in simple and adequate form the principles of hemolysis and the technique of the Wassermann reaction. It gave in a clear-cut manner the gist of an enormous literature and the results of Dr. Noguchi's own researches. The second edition amplifies these principles by describing each factor with their intimate quantitative relations, their meaning, significance, and the sources of error. He shows the necessity for a quantitative control of every factor. The need of fixed standards of practical constancy, and the means of arriving at those constants, he emphasizes and carefully describes. Reviewing the original Wassermann reaction and the more prominent modifications, he briefly classifies them according to the hemolytic system used and the source of the complement, pointing out in every case the possibilities of error. The preparation of the reagents, the technique of the Wassermann reaction, and of

his own modification, and the methods of standardizing each factor of the test and of quantitatively estimating the antibody content of a serum by a titration of the diagnostic dose are described and made clear by charts. Each possible error is now considered and the means of discovering and correcting it described. The quantitative changes due to inactivation were experimentally studied and a curve of gradually decreasing antibody content plotted out.

The later chapters condense much literature into tables made up of cases from all stages of syphilis, of conditions where syphilis is of possible etiological importance, and of controls from practically all fields of medicine. The cases are tested with Wassermann or Noguchi reaction or both. Some few studies were made upon the effect of treatment with mercury or "606." In these last cases the actual number of syphilitic antibodies were determined before and after the injection. In every case a diminution of antibody content was demonstrable by titration, but in many cases not seen with the diagnostic test.

The technique of the butyric-acid test, both for blood and spinal fluid is included, noting the parallelism to cell count in cases of parasyphilitic disease. This has considerable value in psychiatry although not specific for syphilis.

The book ends with a glossary for all the new terms and a rather full bibliography. It amply fulfills the idea of Dr. Noguchi for a serviceable laboratory book and gives enough clinical data to make it interesting also to the internist.

The book is primarily concerned with Dr. Noguchi's methods and does not give quite as much prominence to the Wassermann reaction itself which is still, today, the more popular reaction.

E. P. C. W.

---

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. I, No. 3. Pp. 174; 61 illustrations. Philadelphia and London: W. B. Saunders Company, June, 1912.

THE June number of the *Murphy Clinics* contains, as have the previous issues, clinical lectures on various subjects of modern interest. Surgery of the bones and joints, of the nerves, tuberculosis of the peritoneum, cystic goitre, hypernephroma, cholelithiasis—these are the topics which are discussed at greatest length. Of special interest are the numerous skiagraphs showing the condition of the bones before and after operation in many different cases. The results of arthroplasties of the hip and knee are shown, and the extent of function which is regained by the patients is demonstrated by photographs, and is sufficient evidence of the success of the operative technique.

Then there is a case of rupture of the brachial plexus which is of much interest, though as usual the reader derives more information from the reasoning by means of which a correct diagnosis is reached than from the details of operative technique which are clouded rather than clarified by the stenographic report of Dr. Murphy's remarks during the performance of the operation.

Several of Dr. Murphy's clinical lectures are further elucidated by comments by specialists who have been called in consultation. Thus Dr. Richard J. Tivnen discusses the laryngological aspects of goitre; Dr. Bransford Lewis speaks on the diagnosis of kidney lesions in connection with the case of hypernephroma; and Dr. Charles L. Mix makes some remarks concerning "typhoid spine," though the diagnosis in the present instance does not seem very positive. Dr. Mix also discusses the symptoms presented by the patient who was operated on after a diagnosis of Extradural Hemorrhage from Trauma; this patient had been injured twelve years previously, and the operation was undertaken to relieve progressive mental deterioration, with spastic hemiplegia. The treatment consisted in excision of the dura which overlay the diseased Rolandic region of the cerebrum, and replacement of the osteoplastic flap. Incidentally, Dr. Murphy recommends ligation of the external carotid as the best treatment for rupture of the middle meningeal artery.

The "Five Diagnostic Methods of John B. Murphy," which are inserted at the end of this number of the *Clinics*, are reprinted from an article published in 1910 by Dr. Guy G. Dowdall, and therefore are the "exception which proves the rule" laid down so often by the publishers in their italicized advertisements that "everything is new, never having appeared in print before."

A. P. C. A.

---

NEPHRITIS. AN EXPERIMENTAL AND CRITICAL STUDY OF ITS NATURE, CAUSE, AND THE PRINCIPLES OF ITS RELIEF. By Dr. MARTIN H. FISCHER, Eichberg Professor of Physiology in the University of Cincinnati. The 1911 Cartwright Prize Essay of the Association of the Alumni of the College of Physicians and Surgeons, Medical Department of Columbia University, New York. Pp. 203; 30 illustrations. New York: John Wiley & Sons, 1912.

A REVIEW of this book must take into consideration, the fact that there is here advocated an iconoclastic theory quite at variance with our preconceived notions and almost opposite to the therapy of today. Lacking data by which to judge it, however probable or improbable its tenets may appear, finality of opinion should be reserved.

To his own satisfaction at least, Dr. Fischer has reduced the complicated and antagonistic phenomena of nephritis to a basis so simple as to suggest that such an hypothesis should have been offered and tested ere this. On page 2 of his book, Dr. Fischer, for the sake of clarity in argument anticipates his general conclusions as follows:

"All the changes that characterize nephritis are due to a common cause—the abnormal production or accumulation of acid in the cells of the kidney. To the action of this acid on the colloidal structures that make up the kidney are due the albuminuria, the specific morphological changes noted in the kidneys, the associated production of casts, the quantitative variations in the amount of urine secreted, the quantitative variations in the amounts of dissolved substances secreted, etc."

At last analysis, Dr. Fischer's evidence for this view consists very largely of analogies drawn from the behavior of gelatin and fibrin. When placed in fluid media of various reactions, and in proportion as they swell or dissolve or are influenced by salts present and so on, he feels justified in deducing a similar behavior on the part of the kidney. That this is an entirely sound method of reasoning and that the conclusions so reached are dependable, is open, of course, to question and indeed were it not that Dr. Fischer cites experiments on animals in which nephritis is induced and alleviated and experiments on humans in which the symptoms of nephritis are relieved or dissipated, one could disregard much of the argument. Dr. Fischer's analogies may be correct, but they serve to illustrate his hypothesis and not to prove it.

The experiments *in vivo*, however, in which he applies the simplest of measures as causative and curative, must be taken, on their face value, as remarkable and mark, if true, a long step in the solution of these conditions. Their repetition and acceptance by other workers must be awaited with interest.

In justice to Dr. Fischer, it must be candidly said, that should he prove correct in even a part of what he advocates, as is not inconceivable, he will deserve well, and it is further to be borne in mind that this may prove not the first instance in medicine where the forest has been hidden by the trees. Dr. Fischer has a faculty of turning the experimental data of others to his own account. even when advanced in seeming contradiction of his own views, but he has at least the courage of his convictions and does not hesitate to postulate in this difficult field where any radical move is sure to encounter opposition.

The author has a rather commendable clarity and vigor of style which make the text easy reading and the English is sufficiently within the bounds of good usage to pass muster.

The illustrations, which are quite numerous, are in large part photographic reproductions, and the publisher's work in general has been well done.

R. P.

DIE ERKENNUNG DER PSYCHOPATHISCHEN KONSTITUTIONEN (KRANKHAFTEN SEELISCHEN VERANLAGUNGEN) UND DIE ÖFFENTLICHE FÜRSORGE FÜR PSYCHOPATHISCH VERANLAGTE KINDER. By PROFESSOR DR. TH. ZIEHEN, Geh. Med., Rat Direktor der Psychiatrischen und Nervenlinik der Kgl. Charite in Berlin. Pp. 34. Berlin: S. Karger, 1912.

THIS little paper of 34 pages should be translated into English and distributed among all intelligent men and women, for it applies as well to American as German social conditions. It deals with that class of psychopathic children in which are included not the idiots, imbeciles, feeble-minded, or insane, but those children who are morally weak and who sooner or later come within the pale of the law. Such children may have bad heredity, some injury at birth with possible concussion of the brain, early use of alcohol, or some infectious disease which has caused encephalitis. At any rate, these are the children who early in life begin to steal and lie, learn slowly, and for one reason or another are called bad by their parents and teachers, and who sooner or later come under the influence of the law. As boys or young men they become thieves, and finally land in jail, while the girls become prostitutes. Professor Ziehen, and there is no one better qualified, discusses their ever-increasing number and deplures that there is so little done for them. Even in that land of progress there is no special school where these psychopaths can be placed, and this paper is really a plea for the establishment of such institutions.

The reviewer for many years has been called upon by the House of Detention of Philadelphia to examine the nervous and mental condition of children arrested for various causes. It has always been a question as to where to put these children. They are neither epileptic nor feeble-minded, and therefore cannot be put in such institutions. Private homes are not open to them, and therefore the only place left is the Home for Incurable Children, in which they learn many things they should not, and after a number of years in the majority of instances are worse off than when they first entered. Instead of building jails it would be vastly better if the State built training schools or camps in which such children could be properly educated and trained to be useful citizens and to have a proper respect for the law. What a vast saving it would be, after all, to the State if this were done, for it would save the expense of their trial and incarceration in jail, and what a great thing it would be for the children who are not to blame, for nearly always it is because they have not had the proper care or the environment to keep them from being criminals. What a curious law it is which should take care of the criminal, but which does nothing to prevent the criminal; and what a curious civilization it is which spends millions upon educating the savage, but nothing upon educating the children who live at its back doors. T. H. W.

GRUNDRISS DER HAMATOLOGISCHEN DIAGNOSTIK UND PRAKTISCHEN BLUTUNTERSUCHUNG; EIN LEITFADEN FÜR ANFANGER, STUDIERENDE UND PRAKTISCHE AERZTE. By A. PAPPENHEIM. Pp. 264; 8 colored plates. Leipzig: Klinkhardt.

ALTHOUGH covering 264 pages, many of which are in fine type, the author makes a point of the fact that his book is a "guide." The preface states that the work is founded on the author's course of lectures and that it is his intention to present the subject briefly, avoiding lengthy discussion of matters that still are in doubt and simply presenting those features of theoretical morphology and cytogenesis that are necessary for an understanding of clinical diagnosis. An introduction, eight pages in length, discusses splendidly the limitations of hematology and its relation to medicine in general. The author emphasizes the fact that the alterations of the blood are most frequently simply associated symptoms of a disease whose most striking effects are seen elsewhere than in the blood, and that diseases of the hematopoietic system and the blood itself form a very distinct minority of the conditions studied by hematologic methods.

The book is divided into two parts, the first dealing with hematology in its general and theoretical aspect, the second describing the technique of hematologic examinations. Thus, Part I takes up the chief cell types of normal blood and briefly states the most modern views as to their genesis. This is followed by a description of their pathological variations accompanied by sufficient discussion of hematogenesis to make clear the origin of the pathological types. Not only are variations in morphology discussed, but the quantitative relations of blood elements to one another in pathological states also are considered. Part Ia deals with the theory and theoretical pathogenesis of anemias, leukocytoses, and leukemias in the order of the author's classification of these conditions. This is followed by a discussion of the worth of the various hematologic symptoms in the light of their pathogenesis, and the matter concluded with a discussion of the clinical interpretation of the information acquired by hematologic methods.

Part II, devoted to the actual technique of the blood examinations, describes in thirty-eight pages several methods of estimating the percentage of hemoglobin, counting the cells, and making stained preparations for differential counting. Following this and really in the form of an appendix to the book, are eight beautifully colored plates diagrammatically illustrating the blood pictures of several morbid conditions. Aside from these excellent plates the book is poorly illustrated, there being but a few wood cuts and diagrams which serve almost no purpose in clarifying the text or beautifying the book.

The book, as a whole, is poorly balanced, the theoretical dis-



cussion occupying a number of pages far in excess of the space devoted to technique, a feature that seems faulty in a work purporting to be a guide for beginners. The two parts taken individually show a fine sense of proportion, each subject being given an amount of consideration quite in ratio to its importance.

Throughout the book the most important points are printed in large type, features of especial interest being emphasized by the use of black-faced type. Detailed discussions and relatively unimportant points are printed in fine type, so that the hasty reader, omitting these parts, can get the substance of the writer's meaning by limiting himself to the reading in large type.

In criticism of Part II, on technique, it may be said that the brevity of presentation excludes from consideration numerous well-established and useful procedures, this being particularly true of the staining methods, in which field the author limits himself to a description of his own modification of the combined May-Giemsa methods. If, however, the reader simply desires a series of dogmatic directions for making the essential determinations of the conditions of the blood, this part of the book will be found amply sufficient.

At the beginning of the book, there is found the usual "Inhaltsverzeichnis," but the work suffers considerably from the complete absence of an alphabetical index to its contents, a feature which would add much to the value of the book to the "beginner, student, or practising physician" who chooses it as his "guide." H. T. K.

---

RECENT ADVANCES IN HEMATOLOGY. By WALTER K. HUNTER, M.D., D.Sc., Fellow of the Royal Faculty of Physicians and Surgeons: Lecturer and Examiner in Practice of Medicine. Glasgow University. Pp. 119; 1 colored plate. New York: William Wood & Co., 1912.

THE book consists of a series of three lectures, the Dr. James Watson Lectures for 1910 delivered before the Royal Faculty of Physicians and Surgeons of Glasgow. They originally appeared in one of the medical journals of Scotland, and although there evidently was a demand for them to appear in book form, the author apparently hesitated in bringing them out in a collected series, but later yielded to these demands. The advisability of this step cannot be questioned; as the author had compiled a thorough and complete book dealing with some of the recent advances in hematology.

Lecture I consists of a description of the morphology of the blood together with the methods of testing the various chemical and physical properties of blood. In Lecture II the origin and theories

of origin of the cellular constituents of the blood is first considered. The pathological picture of the changes that take place in the bone marrow and lymphatic tissue in diseases of the blood is also considered in this lecture. The latter part of Lecture II and all of Lecture III is a consideration of the various forms of anemia and leukemia, purpura, hemophilia, and allied diseases. These diseases are not treated in any systematic or exact method. Particular attention is paid to the pathogeneses and etiology of the disease under consideration; but aside from this there is simply a random discussion of the newer phases of the disease. Symptoms are occasionally noted. Treatment is only mentioned in connection with hemophilia and leukemia. The author says but little advance has been made in the treatment of the latter disease and that the Röntgen ray treatment produces only temporary improvement, lasting for a year or two at the most. Apparently he is unaware of the splendid results achieved in this country by the  $x$ -ray treatment. The book is completed by an appendix dealing with the preparation and method of employing a few of the more valuable stains for blood films.

J. H. M., JR.

---

A LABORATORY GUIDE IN BACTERIOLOGY FOR THE USE OF STUDENTS, TEACHERS, AND PRACTITIONERS. By PAUL G. HEINEMAN Ph.D., Associate in Bacteriology, University of Chicago. Second Edition, Pp. 210; 36 illustrations. Chicago: University of Chicago Press.

THE second edition of this excellent technical guide in bacteriology has been considerably enlarged by the addition of chapters on subjects pertaining to the recently separated specialty of public health. In the preface the author indicates a rearrangement of subject matter to permit of ready reference. Prof. E. O. Jordan supplies the introduction. The subjects covered comprise technique, general bacteriology, including an introduction to the various groups of bacteria, admirably arranged for a proper conception of the relations they bear to one another, and bacteriological examinations of water, sewage, milk, and soil, while the final section concerns the methods of study of yeasts and moulds.

The work presents a course as given by Heineman at the University of Chicago, and apparently includes the methods he believes feasible to teach to students. The methods for analysis in regard to public health are excellent, and while some are still *sub judice* with the profession, the student will obtain a clear understanding upon which to form a later judgment. A technique for mycology is not often included in bacteriological books, and is welcome here. Incidentally, the instructions for students' behavior in the laboratory are excellent. This enlarged edition will be gladly received by those conducting similar courses. H. F.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**The Phthalein Test. An Experimental and Clinical Study of Phenol-sulphonephthalein in Relation to Renal Function in Health and Disease.**  
—L. G. ROWNTREE and J. T. GERAGHTY (*Arch. Int. Med.*, 1912, ix, 284) describe their technique of injecting and measuring the excretion of phthalein, using 6 mgms. subcutaneously, intramuscularly, or intravenously, and recording the time of appearance of the drug, and the amount excreted in the urine in one and two hours. This is done by the Duboscq colorimeter, their modification of the Autenrieth-Konigsberger colorimeter, or by graduated cylinders. Excretion in health following different methods of administration has been studied in detail. Experimentally the time of appearance was shortest after intravenous injection and more rapid following intramuscular than subcutaneous. In humans Rowntree and Geraghty believe that absorption plays a small role when one hour determinations following intralumbar injections are employed. The average output is 57.5 per cent. Administration into the lumbar muscles is the method of choice. Experimentally, the influence of diuretics was studied. It was found that those drugs which stimulate the secreting cells, slightly increase the phthalein output, while those which act by changes in blood or osmotic pressure have no effect. In patients, no appreciable difference in output could be detected with the therapeutic dose of common diuretics. Since the kidney shows a specificity for phthalein, it was attempted to discover to which part of the kidney this action belonged. By using the renal system in frogs, it was shown that phthalein could be excreted by the tubules. Presumably this is true of mammals. In experimental acute tubular nephritis, there is marked diminution in output, while there is

little diminution in the early stages of the acute vascular nephritis. Hence Rowntree and Geraghty conclude that the glomeruli play a subsidiary part in the excretion of the drug. Five cases of acute nephritis were studied. There was a marked decrease in phthalein output when the clinical condition was grave. Twenty-five cases of chronic parenchymatous nephritis were studied. In mild cases very little disturbance of function was indicated. But where the drug is excreted in traces or not at all, a grave prognosis should be given though no signs of uremia exist. Twenty-three cases of chronic interstitial nephritis were studied. The test proved of immense value in revealing the degree of destruction of renal substance, and demonstrated itself to be of extreme importance for diagnosis and prognosis. Twenty-five cases of uremia were studied. In all, for two hours the phthalein elimination was zero or a faint trace. Thirty-three cases of broken compensation or in which cardiac insufficiency was associated with varying grades of true nephritis were studied. Rowntree and Geraghty found that decrease in function accompanies marked passive congestion without nephritis, but as the condition improves the phthalein output increases. Rowntree and Geraghty believe that in cases of obstruction of the lower urinary tract, a marked decrease in phthalein output invariably means severe derangement of renal function. The test, in conjunction with the clinical condition is of more value than the study of total urine, solids, nitrogen, and urea. Rowntree and Geraghty describe the technique of the phthalein test as applied to estimation of the function of the individual kidney by means of ureteral catheterization. In no instance was there inhibition of function as the result of this to seriously interfere with the value of the test. In unilateral disease in proportion to the decrease in function on the diseased side, approximately there was a proportionate increase in function on the healthy side. In bilateral disease it was possible to determine the individual function of each kidney and whether it was normal, less, or greater than normal. On the whole, Rowntree and Geraghty believe that phenolsulphonaphthalein is better adapted for use as a functional test than any other drug previously employed for this purpose, on account of its early appearance in the urine, and the rapidity and completeness of its elimination by the kidney.

---

**A Method of Reducing Excessive Frequency of the Heart Beat, by Means of Rhythmical Muscle Contractions Electrically Provoked.**—W. HAMPSON (*Proc. Roy. Soc. Med.*, 1912, v, 119), reports that the stimulation of muscles by means of pulsating electrical currents causing alternate contraction and relaxation have a beneficial action on their development. The Bergioné system allows for the passage of current through large muscle areas without discomfort. Schott's method of treatment for suitable cardiac cases by properly graduated exercise has long been familiar. The application of these principles in heart disease produces results of interest and importance. Muscular contraction squeezes out blood from the veins towards the heart, the action of the valves securing its passage in the right direction. The subsequent relaxation allows the veins to fill and receive more blood than if they had not been so completely emptied. Thus the muscles become a modified heart. If the muscular contractions are made nearly synchronous with the heart beat by electrical stimulation, the artificial

waves of blood pressure in the venous system reinforce the heart action coincident with its own impulse. In this way that portion of the stimulation to the heart depending on venous pressure is intensified sufficiently to bring the beats from approximate to exact synchronism with the muscular contractions. By pursuing this line of action, the pulse rate may be markedly lowered. Hampson believes that this method is useful in numerous cases of weak, dilated, or irritable hearts. It increases the pressure on the right side of the heart, producing a better pulmonary circulation to relieve dyspnea; at the same time the heart is relieved of some of the muscular effort necessary to maintain the flow of blood, so that a greater amount of circulation work is done with the heart in a partially resting condition.

---

**Bacteriology and Pathology of the Tonsils with Especial Reference to Chronic, Renal, and Cardiac Lesions.**—DAVID J. DAVIS (*Jour. Infect. Dis.*, 1912, x, 148) reports that the relation of tonsillar infection to lesions existing in other regions, especially in joints, heart, and kidneys, has received much attention from the clinical side. But bacteriological work in such cases is incomplete. Davis has studied 113 hypertrophied tonsils from cases of arthritis, nephritis, endocarditis, and tonsillitis without serious complications, taking smears and cultures from both the surface and crypts of the extirpated glands. Of 25 cases of arthritis, 25 showed hemolytic streptococci as the predominating growth. Seventeen of these strains were inoculated intravenously into rabbits, causing in 15 cases joint lesions and in 1 endocarditis. Of 10 cases of nephritis, 9 showed hemolytic streptococci predominating; 8 of the strains in rabbits caused lesions in joints or tendon sheaths. In all the kidneys and urine showed no abnormalities. Of 10 cases of endocarditis, 6 showed streptococci and 4 pneumococci predominating. Three of the latter group were injected in rabbits, producing in 2 cases vegetative endocarditis. Of 61 cases of tonsillar hypertrophy, 57 showed streptococci predominating. Seven of these strains produced rabbit arthritis as did one, from a case of multiple neuritis without arthritis or endocarditis. The therapeutic results of tonsillectomy furnish the best argument that infected tonsils bear a relationship to arthritic, renal, cardiac, and other clinical conditions. Davis believes that the occurrence in the tonsils of pure streptococci without any other significant germ would seem to point to these organisms as etiological. The reason why in one case nephritis is produced and in another arthritis probably lies in varying local susceptibility of the individual's tissues, rather than in any peculiar specificity of the infecting germs. Finally, Davis believes from his experimental evidence, that streptococci produce arthritis, only occasionally localizing on heart valves, while pneumococci produce arthritis rarely, but frequently localize on the endocardium. This observation was paralleled by the few clinical cases studied.

---

**Abscess of the Lung and Liver. Simple Cure of a Chronic Case by the Upside-down Position.**—W. M. McKECHNIE (*Lancet*, 1912, clxxxii, 865) cites the following case. A boy, aged fourteen years, had coughed up a teacupful of pus night and day for five years. Physical examination showed dulness at the right base continuous with liver dulness.

Over this area the breath sounds were nearly absent, while above moist rales were heard. On the affected side the diaphragm moved only slightly. McKechnie believed the patient had a liver abscess with perforation of the diaphragm and pleura; and was intermittently evacuating the cavities through the bronchi. McKechnie's treatment was as follows: The patient was placed over the edge of a table, head downwards, with the whole body hanging upside down. The legs and thighs on the table, lay at right angles to the trunk and thus supported it. In this position the patient coughed and squeezed until no more pus came out. The maneuver was repeated five or six times daily. In this way at first, the patient got rid of large quantities of pus which rapidly diminished and in six weeks stopped. The general condition improved markedly. McKechnie suggests that this method should be tried in abscess of the lung and bronchiectasis before resorting to the more formidable surgical procedures.

---

**The Blood Picture in Disease of the Glands of Internal Secretion.**—L. BORCHARDT (*Deutsch. Arch. f. klin. Med.*, 1912, cvi, 182) has extended the study of the blood in disease of the glands of internal secretion. Within the last few years diseases of the thyroid gland have been studied in particular. The present observations are of interest in connection with the findings in thyroid disease, because of the similarity of the blood pictures. Borchardt finds that not only in Basedow's disease, but also in all other diseases of the thyroid, hypophysis, and adrenals the blood is characterized in the majority of cases by a relative and absolute increase of the mononuclear cells, particularly the lymphocytes. In about half of the cases there is also a leukopenia and eosinophilia is about equally frequent. Similar changes are found in the blood of patients with the clinical signs of status thymolympathicus. Since clinical and anatomical evidence of status thymo-lymphaticus is at hand in many instances of disease of the thyroid, hypophysis, and adrenals, it is possible that the blood picture in such cases is attributable to the status lymphaticus.

---

**A Source of Error in Nylander's Test for Glucose.**—E. STRAUSS (*Münch. med. Woch.*, 1912, lix, 85) found a negative Nylander's test for sugar in the urine of a diabetic, whose urine was shown to contain an abundance of sugar by the Fehling and polariscopic methods. It was found that the patient was receiving injections of iothion (d-iodoxypropan). On adding this substance to diabetic urine or to solutions of sugar, the Nylander reaction became negative, though there was no interference with the reduction of copper. The addition of potassium iodide or iodine is without effect. It appears that the iothion is excreted in the urine as such and forms some combination with the bismuth which prevents its reduction.

---

**Diastase in Urine and Feces.**—A. LINDEMANN (*Zeitschr. f. klin. Med.*, 1912, lxxv, 58) has studied the excretion of diastase in urine and feces, particularly in pancreatic disease. With normal gastric secretion the normal diastatic content of the urine is between 15 and 45 units (Wohlglgemuth's method); that of the feces is about 200 units. In anacidity of the stomach the diastase of the urine and feces is

moderately increased. It is probable here that Wohlgemuth's suggestion that the salivary diastase, escaping destruction in the stomach, accounts for the increase, is correct. With hyperacidity normal values are again found. Continuous hypersecretion of the stomach, whether accompanied by hyperacidity or not, is usually associated with a similar hypersecretion of pancreatic juice. In this condition the urine may contain 50 to 800 units of diastase, with simultaneous increase of fecal diastase to 2000 units and more. This shows that examination of the urine alone may lead to error, since increase of diastase occurs with gastric hypersecretion as well as with diseases of the pancreas. There is, however, this important difference: While with pancreatic disease, the amylolytic enzyme of the feces is totally lacking or present only in traces, with gastric hypersecretion fecal amylase is very greatly increased. It is evident, therefore, in the application of this diagnostic procedure that determinations of diastase should be made on both urine and feces in doubtful cases.

**A New Method for the Determination of Total Nitrogen in Urine.**  
—O. FOLIN and C. J. FARMER (*Jour. Biol. Chem.*, 1912, xi, 493) describe a method for determination of total nitrogen in the urine, which, in principle, is a microchemical method based on the Kjeldahl-Gunning process for decomposing nitrogenous materials and on the methods of Nessler and of Folin for the determination of ammonia. *Method:* "Five c.c. of urine are measured into a 50 c.c. measuring flask if the specific gravity of the urine is over 1.018, or into a 25 c.c. flask if the specific gravity is less than 1.018. The flask is filled to the mark with water and inverted several times to secure thorough mixing. One c.c. of the diluted urine is then measured into a large test tube made of Jena glass (size 20 to 25 mm. by 200 mm.). To the urine in the test tube add 1 c.c. of concentrated sulphuric acid, 1 gram of potassium sulphate, 1 drop of 5 per cent. copper sulphate solution, and a small, clean quartz pebble (to prevent bumping). Boil over a micro-burner for about six minutes, *i. e.*, about two minutes after the mixture has become colorless. Allow to cool about three minutes, until the digestion mixture is beginning to become viscous (it must not be allowed to solidify). Then add about 6 c.c. of water, at first a few drops at a time, then more rapidly, so as to prevent the mixture from solidifying. To the acid solution is then added an excess of sodium hydrate (3 c.c. of saturated solution) and the ammonia is aspirated by means of a rapid air current into a measuring flask (volume 1000 c.c.) containing about 20 c.c. of water and 2 c.c. of  $\frac{n}{10}$  hydrochloric acid. The air current used for driving off the ammonia may well be rather moderate for the first two minutes but thereafter for eight minutes should be as rapid as the apparatus can stand. Now disconnect, dilute the contents in the flask to about 60 c.c., and dilute similarly 1 mgm. of nitrogen in the form of ammonium sulphate, to about the same volume in a second measuring flask. Nesslerize both solutions as nearly as possible at the same time with 5 c.c. of Nessler's reagent diluted immediately before hand with about 25 c.c. of water. (Five c.c. of Nessler's reagent gives the maximum color with 1 to 2 mgms. of ammonia, and when diluted as indicated, turbidity is avoided.) The color produced does not react the maximum till the

end of about half an hour, but the increase is small and is immaterial to the result when the reagent is added as described, *i. e.*, practically simultaneously to the standard and to the unknown ammonium salt solution. The two flasks are therefore at once filled to the mark with distilled water, mixed, and the relative intensity of the colors is determined by means of a colorimeter . . . The reading of the standard divided by the reading of the unknown gives the nitrogen in milligrams in the volume of urine taken." For further details, the original should be consulted. The ammonium sulphate used as the standard must be be specially prepared, as described by the authors.

**The Radiologic Examination of the Apices of the Lungs. The "Cough Phenomenon."**—S. KRENFUCHS (*Münch. med. Woch.*, 1912, lix, 80) refers to the well-known facts that apices of individuals with long thorax and wide intercostal spaces are clear in health, whereas with a short thorax and narrow interspaces there is usually a shadow over the apices on radiologic examination. In the latter instance it is claimed by some that the shadows disappear during deep respiration, though Krenzfuchs finds such a result exceptional. He has noted, however, that normal apices, which cast shadows—whether from atelectasis or from the conformation of the thorax—become clear when the patient coughs. This clearing of the apices during cough he designates the "cough phenomenon." (*Hustenphänomen*). The explanation of the phenomenon is as follows: The deep inspiration preceding the cough fills the lower parts of the lungs. With the cough, the contracture of the abdominal muscles and the passive elevation of the diaphragm force the air into the apices of the lungs, since the glottis is closed. Inflation of the apices is the result. The examination is made with a soft tube and weak current. During cough, the head is turned away from the apex examined, when the antero-posterior position is used. The value of the "cough phenomenon" is chiefly in the differentiation between atelectatic and infiltrated apices. The former become clear during cough, while the latter remain dark or clear only partially.

**On the Determination of Ammonia in Urine.**—O. FOLIN and A. B. MACALLUM (*Jour. Biol. Chem.*, 1912, xi, 523) have devised a new method for the quantitative estimation of ammonia in the urine. "Into a test tube measure by means of Ostwald pipettes 1 to 5 c.c. of urine. (The volume taken should give 0.75 to 1.5 mgms. ammonia-nitrogen. With normal urine 2 c.c. will most often give the desired amount. With very dilute urines 5 c.c. may be required, while with diabetic urines rich in ammonium salts even 1 c.c. may give too much, and the urine must be diluted). Add to the urine a few drops of a solution containing 10 per cent. of potassium carbonate and 15 per cent. of potassium oxalate, and a few drops of kerosene or heavy, crude machine oil (to prevent foaming). Pass the strong air current through the mixture for ten minutes (or as long as is necessary to drive off all the ammonia) and collect the ammonia in a 100 c.c. measuring flask containing about 20 c.c. of water and 2 c.c. of  $\frac{N}{10}$  acid. Nesslerize as described under total nitrogen and compare with 1 mgm. of nitrogen obtained from a standard ammonium sulphate solution and similarly Nesslerized."



## S U R G E R Y

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**Further Experiences with the Treatment of Volkmann's Ischemic Paralysis and Contraction by the Method of Robert Jones.**—SAYRE (*Amer. Jour. Orthop. Surg.*, 1912, ix, 557) summarizes his conclusions as follows: Volkmann's ischemic paralysis is the result of a myositis set up by obstruction to the supply of oxygen by pressure either by bandages, splints, or sometimes by position and pressure of the bone fragments. Shortening of the affected muscles results, the muscles of the forearm being those usually affected, those of the hand occasionally. Massage is too intermittent to produce good results. Shortening of the bones and removal of scars pressing on nerves have given good results. Jones' method of constant traction on contracted muscles produces results when massage fails, as it is a constant instead of an intermittent force. In some cases bone growth at a faster rate than muscle growth may cause recurrence of the deformity in a way analogous to the recurrence of equinus in cases of paralysis of the leg, and a second stretching may then be necessary.

**Pyelotomy in Renal Calculi.**—BAZY (*Jour. d'Urol.*, 1912, i, 739) adds 3 interesting cases to those which he has previously reported. The calculi were large and ramifying, the only kind which, in Bazy's opinion, deserve publication, the small calculi being of only secondary interest. He insists that the radiograph will locate the calculus and determine in advance if a pyelotomy or nephrotomy is indicated. Every calculus, the internal border of which, according to the radiograph, is less than 5 cm. from the median line, is in the renal pelvis. Those situated more externally, are in the kidney substance. The shadow of the calculus should be at the level of the third lumbar spine or the junction of the second and third. The shock of pyelotomy is reduced to a minimum and the hemorrhage is slight. It is the incision into the kidney substance which bleeds freely, and in some cases the hemorrhage has been so abundant as to call for a nephrectomy. More frequently than some authors believe, a fatal secondary hemorrhage has taken place. Even if renal calculi cannot always be removed by a pyelotomy, they can be removed by this means more often than is thought, and Bazy can remove some by this method which are in the renal parenchyma. Pyelotomy permits lavage of the pelvis for infection,

which a nephrotomy does not, since the pelvis is being compressed with the vessels for hemostasis. Bazy calls pyelotomy the operation of choice for the removal of renal calculi, nephrotomy the operation of necessity.

---

**The Mode of Origin of Renal Tuberculosis.**—**RAFIN** (*Jour. d'Urol.*, 1912, i, 779) studied 160 cases upon which he did a nephrectomy for renal tuberculosis, to determine the clinical or apparent beginning of the disease. In 99 of the cases, or 61.87 per cent., the first symptoms were vesical, and these he therefore called the signal-symptoms. Renal pain, vague heaviness, torture, or more rarely painful crises simulating renal colic; less often mark the beginning of the affection. They are important, however, because while more fugacious than the vesical symptoms, less troublesome, and less characteristic, they annoy the patient so little that he ascribes them to some rheumatic affection, or to a cold, a movable kidney, etc., and in consequence neglects or forgets them. For this reason they may be the first symptoms of the disease more frequently than the patients state. In a small number of cases, hematuria will be the first symptom noted. Exceptionally, an analysis of the urine reveals the presence of albumin as the first sign of the disease, or the patient perceives that the urine is turbid. It is exceptional for the patient first to observe a disturbance of his general condition. It is often striking to observe the contrast between the grave renal lesions and the preservation of a good general condition.

---

**A New Operation to Reestablish the Continuity of the Intestine after an Extensive Resection of the Sigmoid and Rectum.**—**VIGNOLI** (*Archiv. gén. d. chir.*, 1912, vi, 621) proposes a method of reestablishing the continuity of the bowel after a considerable portion of the rectum and sigmoid have been removed, by grafting between the two remaining cut ends of the large bowel, a corresponding portion of the lower ileum. He first carried out experiments on dogs to demonstrate its feasibility and to perfect its technique. Later he performed the operation on the cadaver to adapt it to the different anatomical conditions in the human. Still later came the opportunity to practise the operation on a live patient. In describing the technique, he emphasizes first the necessity of choosing a portion of the ileum which from the position of its mesentery, will permit it to best fit into the position it is intended to occupy. The mesentery attains its maximum length at about 40 cm. from the end of the ileum, nearly in the line of the superior mesenteric artery. The portion to be excised extends from this point upward and to the left. After dividing the ileum at the desired levels and the mesentery in radiating lines from the same points, at the lower end the mesentery is incised in the line of the intestine for 2 or 3 cm. and about 4 cm. from the intestine, in order that the excised portion of intestine can be straightened out. The continuity of the small intestine is then reestablished by a circular enterorrhaphy and the cut edges of the mesentery brought together by a few sutures. The colonic end of the large bowel excised with the growth and the rectal end are fixed in their respective positions to the posterior abdominal wall by sutures. The portion of ileum transplanted into the gap is anastomosed at the colonic end of the divided

large bowel by a circular enterorrhaphy. A lateral anastomosis may be made, so that the open end of the colon may be employed for an artificial anus. At the rectal end after a preliminary preparation of the rectum, the lower end of the piece of small intestine is invaginated into it and fixed there by sutures. In the case operated on it was necessary to make a preliminary cecostomy, in order to allow free escape of the feces and relieve the toxemia, and to permit rest of the diseased portion of the bowel as well as local treatment. The ablation of the stenosed portion of the rectum and sigmoid was performed at another time, and the enteroplastic operation at a still later period. The patient did well after the operation, but died of metastatic recurrence of the disease after leaving the hospital.

**The Operative Treatment of the Edema of Elephantiasis.**—KONDOLEON (*Zentralbl. f. Chir.*, 1912, xxxix, 1022) refers to the work of Mikulicz, Lanz, and Handley for the removal of persistent edema. Lanz tried to establish a new collateral circulation in the thigh by strips of fascia passed into holes made in the femur and cutting multiple small holes in the fascia lata. Handley proceeding from the view that the sclerotic edema in the upper extremity in the later stages of mammary carcinoma was due to the obliteration of the lymph paths, attempted to make new paths for the obstructed lymph by means of silk threads from the hand to the loose subcutaneous tissue of the thorax. In a case of sclerotic edema from a crushing wound, Kondoleon modified the Lanz procedure by laying the fascial strips between muscles and leaving the ends of the fascial incision open. This method of making a communication between the subcutaneous tissue and muscles was carried out further in cases of elephantiasis. He found conditions during his operations for this condition which convinced him that neither the Lanz nor the Handley methods could be of service in elephantiasis. In every old case and independent of the cause of the hard edema, he found besides the known changes in the skin and subcutaneous tissues, the fascia always much thickened (up to 3 cm.), thickly infiltrated, adherent to the surrounding tissues, especially to the fatty tissue lying between the skin and fascia. The upper surface of the aponeurosis was irregular, and of milky appearance. Its under surface lying on the muscle had its normal smooth color and consistency. In some cases he could separate the fascia from the connective-tissue layer between the subcutaneous fatty tissue and the fascia. In other cases this layer could not be separated from the aponeurosis. The greater quantity of the retained lymph came from the region of this thickened aponeurosis. The underlying muscles were found microscopically and macroscopically to be normal. These findings led to the conclusion to make a wider communication between the subcutaneous tissue and muscles and to the development of the following technique: When only the leg was involved, he made two incisions the whole length of the limb, one on the outer and one on the inner side of the leg. When the whole limb was involved, he made four incisions, two in the thigh and two in the leg. The skin is separated and retracted by broad hook retractors. The infiltrated fatty tissue covering the fascia is excised, and the fascia is thus exposed, when a piece of it is removed, the length of the

incision and the width of three to four fingers. The muscles bulge forward. Complete hemostasis is provided and skin sutures introduced without drainage. This operation was performed on 6 cases. In 2 the operation was repeated and in 1 of thirty years' duration, it was done the third time. The technique was changed each time until the above described technique was employed in the third operation, by which a good result was obtained. Not enough time has elapsed to permit definite results, but they are already satisfactory and prove the value of the method.

---

**Supraclavicular Anesthetization of the Brachial Plexus.**—BORCHERS (*Zentralbl. f. Chir.*, 1912, xxxix, 873) says that Schleich's infiltration method of local anesthesia is gradually being displaced by Braun's method of anesthesia produced by injecting the large nerve trunks with a local anesthetic fluid, and that not only may we do small operations on ambulatory patients by local anesthesia, but major operations as well. By combining the method with the use of scopolamin, pantopton, morphine, or other drugs, we may do severe operations on very nervous and excitable people. When necessary we can now do such operations on any part of the body. Borchers began to employ the method of injecting the brachial plexus soon after Kulenkampff's first paper on this subject, and is now prepared to report on the results in 35 cases. (For abstract on Kulenkampff's paper, including the technique of the method see the January number of this JOURNAL, p. 134.) Borchers says that Kulenkampff showed before the 1912 surgical congress, and he himself has found, that a puncture of the arterial wall is without importance. According to his experience, the anesthesia comes on in from three to thirty minutes, depending upon the strength of the solution and the distance from the nerve at which the injected fluid is deposited. It occurs more quickly when the nerve itself is injected than when the needle goes through the nerve. The duration of the anesthesia with paresis or paralysis of the muscles is about one and one-half to two hours. Borchers thinks that the degree of paralysis of the muscles will be proportionate to that of the anesthesia. The latter was sufficiently marked to render the most severe operations on the upper extremity painless. Usually the whole arm up to the shoulder girdle is without pain. Occasionally there was some feeling in a narrow strip along the postero-internal side of the arm from the axilla to the elbow, corresponding to the supply of the cutaneous branch of the median nerve. It was observed also that notwithstanding that the operation on the forearm was painless, the application of the Esmarch bandage to the arm was unpleasant. In one case there was observed a palsy of the radial, median, and ulnar nerves, which lasted several weeks and gradually disappeared.

---

**Anesthesia of the Sciatic Nerve.**—JASSANETZKY-WOINO (*Zentralbl. f. Chir.*, 1912, xxxix, 1021) has been working for three years to perfect a technique for the injection of the sciatic nerve with an anesthetic fluid, and he has finally found the point where the nerve can be easily and safely attacked. It corresponds to the junction of a horizontal line passing through the top of the great trochanter and a vertical

line through the margin of the tuberosity of the ischium. In 3 out of 20 cadavers, the horizontal line was from 1 to 1.5 cm. too high. In all the others the junction of these two lines was exactly at the point where the nerve, immediately after making its exit from the great sciatic foramen, lies directly on the bone. Almost without exception, colored gelatin injected at this point was found by dissection either directly over or under the nerve or within the nerve substance. In most of his clinical cases, the injection of the sciatic and anterior crural nerves was combined, and in all operations during the work on the soft tissues the anesthesia was complete. During the manipulations of the bone, as in lifting the periosteum or sawing the bone, considerable sensibility remained. In the more recent cases, he has injected, not 10 but 15 to 20 cm. of the novokain solution with 7 to 10 drops of adrenalin, and in this way he obtained an anesthesia complete enough to permit him in a man, aged seventy-eight years, to amputate the anterior portion of the foot for gangrene. The technique of the injection is as follows: The patient is placed in the prone position and the point for the injection is determined as above stated. An 8 cm. long needle is introduced at right angles to the surface down to the bone. When the bone is not struck, the needle is tried somewhat higher or further outward from this point. When the needle strikes the bone it is withdrawn a few millimeters and 10 c.c. of a 2 per cent. novokain-adrenalin solution is injected for operations on the soft tissues, 15 to 20 c.c. for operations on the bone. In the former cases, the operation may be begun after a half hour, in the latter not sooner than an hour after the injection. This method was employed in 12 cases. In only 1 did no anesthesia develop. In all the others, however, the soft tissues were anesthetized completely and the bones in varying degrees. In most cases it will be necessary to inject the anterior crural nerve also as L  wer advised. The skin supplied by the obturator nerve is so small in area that it can be injected with a small quantity of the fluid.

---

**Investigations Concerning Surgical Methods of Treatment for Trigeminal Neuralgia.**—OTTO (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 78) considers that the justification of the operative treatment for trigeminal neuralgia is generally recognized, but that just which operation should be done in a given case is not an easy question to decide. Neither the peripheral operations nor the resections at the base of the skull, will always give permanent relief. Even the extirpation of the ganglion in many cases gives only temporary relief, probably because of incomplete operations. Only rarely do we find the seat of changes in the nerve and the mode of origin of the neuralgia is rarely determined. Nor do we know whether the neuralgia is due to functional or organic disease. As the result of his studies, Otto believes that the peripheral operations are frequently followed by recurrence. Thiersch's nerve exeresis in most cases leads to recurrence, very frequently after a few months. The condition recurs more rarely after resections at the base of the skull. Extirpation of the Gasserian ganglion gives the best results, provided the ganglion is wholly removed. The operation is, however, technically difficult and should be reserved for otherwise hopeless cases and especially for those in which the three

branches of the ganglion are involved. Under these circumstances, one is fully justified in trying out the injection method of combating the affection. Alcohol (70 to 80 per cent.) is the most suitable fluid with which to inhibit the conductivity of the nerves without damaging the other tissues. The deep injection at the base of the skull suffices even in severe cases to anesthetize the regions supplied by the treated branches for months, and it can be repeated without danger. The effect usually lasts a long time, but whether a permanent cure may result remains to be proved. The Offerhaus method is favored because it is easily performed without previous practice. It is without danger, and may be employed to obtain anesthesia for the performance of operations in the trigeminus regions.

---

**End Results of Fracture of the Shaft of the Femur.**—ESTES (*Annals of Surgery*, 1912, lvi, 162) summarizes the conclusions on 760 tabulated cases of fracture of the shaft of the femur as follows: The records of fractures are kept very incompletely and it is quite impossible in the United States to obtain anything like full, accurate, and reliable data of a large number of finished cases. The largest number of cases of fracture of the shaft of the femur occurs in men aged between twenty and fifty years. Children aged under ten years have the next largest number. Working people furnish the largest number of cases, though data in regard to this point are not kept in the majority of cases. Indirect violence produces by far the largest number of these fractures. Of the reported cases, the middle third of the bone is most frequently broken, the lower and upper thirds are almost equally involved. Simple fractures far outnumber the compound and complicated ones. The average shortening before reduction is 1.38 inch. By far the most frequent method of treatment was by some form of Buck's extension. An anesthetic was not used to assist reducing the fractures in the majority of reported cases. The average weight used in extension was 14 pounds. (This is too little weight.) The average reported shortening of completed cases is one-half an inch. Average length of time in bed, 8.2 weeks. Average length of time incapacitated, 2.7 months. (This is probably a mistake.) Average length of time crutches, canes, or other aids in walking were used, 8 weeks. Limp was present for some time in the large majority of cases. A little more than one-tenth of the cases had excessive callus which produced some disturbance. Nearly all the reported measurements were taken from the anterior superior spine of the ileum to the internal malleolus. Disability estimated by: (a) Endurance, (b) pain, (c) swelling, (d) interference with joint function; present in about 1 case in 25. Death rate of reported cases, 3.69 per cent. (This Estes believes is a mistake.) Chief causes of death: (a) Pneumonia, (b) shock and exhaustion, (c) delirium tremens. Estes' first recommendation and deduction from his work is that teachers in medical schools should give far more attention than they have done in the last decade or more to their own investigations of fractures, and to the teaching of this most important branch of surgery to the students who belong to their classes. Second, while recognizing the fact that x-ray photographs may be most misleading, the writer believes, nevertheless, when taken by competent anatomists who understand the importance of proper

relative position of tube and limb, and the importance of taking more than one view of the fracture, these radiographs will furnish an indication for the proper reduction and the mechanical appliances for the preservation of proper apposition, and they will serve as a graphic record of the fracture itself. Estes finds that in most cases treatment by some form of traction enables the patient to resume his occupation and function without serious detriment. In selected cases, where it is impracticable to restore the fragments to their proper position, and where mechanical means have failed within a reasonable time to produce proper restitution of the fragments, the open method may be employed, but then only by an experienced surgeon, one who habitually employs most thorough aseptic methods. The results may be considered good if the measurements show no more than an inch of shortening, provided there is no inversion or eversion of the foot from angulation of the fragments.

---

## THERAPEUTICS

---

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

---

**The Treatment of Diphtheria Infection by Means of Diphtheria Endotoxin.**—HEWLETT and NANKWELL (*Lancet*, 1912, clxxxiii, 143) tested the effect of diphtheria endotoxin on diphtheria patients of whom many had harbored the diphtheria bacilli for many weeks or months after the acute attack. After one or more injections of the endotoxin all the patients showed definite improvement. In many the diphtheria infection ceased entirely; in some it persisted, and the patient remained uncured; but even in these unsuccessful cases they noted invariably a diminution in the number of bacilli. The endotoxin is prepared by growing a virulent culture of diphtheria bacillus on serum or blood agar, collecting the growth, washing it two or three times in sterile physiological salt solution so as to remove the toxin, grinding the bacterial mass in the presence of intense cold, and filtration of the ground mass through a Berkefeld filter. The filtrate contains the endotoxin and is standardized by the addition of sterile salt solution so as to contain from 2 mg. to 5 mg. per cubic centimeter. With regard to dosage, they first used the endotoxin in doses of from 0.5 mg. to 1.0 mg., but the patients did not do so well as when they gave an initial dose of 2 mg. At the end of a week or ten days, if the culture was still positive, a second injection of 5 mg. was given and this, if necessary, was repeated later. The dose was the same for children and adults. No ill effects, except some redness and tenderness around the site of injection, followed the administration of the endo-

toxin. Only one patient showed any general disturbance, and that merely by a transitory rise of temperature and a feeling of malaise. Hewlett and Nankwell give details of 24 cases treated by this method. They advise the use of endotoxin as an aid to the antitoxin treatment, and consider that its greatest value lies in the reduction of the number of possible diphtheria carriers.

---

**Collapse Produced by Hormonal.**—ZUELZER (*Deutsch. med. Woch.*, 1912, xxxviii, 1233) advances an explanation for the symptoms of collapse reported by many different observers as occurring after the intravenous administration of hormonal. Zuelzer says that hormonal had been given over a period of two years by the intravenous method over 4000 times without any untoward effects. Then, suddenly, reports of marked collapse after the administration of hormonal began to appear in the literature, including one fatal case. Zuelzer was inclined at first to attribute these untoward results to technical faults in the administration. His practise always has been to allow the hormonal to enter the vein very slowly, drop by drop. However, with all technical precautions on his part, he had 4 cases of collapse in quick succession in his own practice. A laboratory investigation of the hormonal on hand showed the presence of an albumose. Zuelzer attributes the toxic action to the substance that appeared to be formed during the process of manufacture. The hormonal now manufactured is free from this albumose, according to Zuelzer. He gives the pulse and blood pressure readings in a few cases after the administration of the new hormonal intravenously that show they were little influenced by the injections.

---

**Report of a Case of Diabetes Insipidus with Marked Reduction in the Amount of Urine following Lumbar Puncture.**—HERRICK (*Arch. Int. Med.*, 1912, x, 1) reports a case of diabetes insipidus in which there were symptoms pointing to a cerebral origin of the disease. A man, aged forty-three years, had for four years the typical manifestations of diabetes insipidus. The urine varied in amount from 7500 to 11,000 c.c., and was always of low specific gravity, 1001. Lumbar puncture was made for the purpose of investigating the cause of the trouble. Less than 5 c.c. were withdrawn, the fluid escaping slowly under low pressure. Within forty-eight hours the daily amount of urine had dropped to 660 c.c. Headache, pain in the back of the neck, anorexia and vomiting, with a feeling of general weakness followed the puncture. Morphine was given for pain and almost no fluid or food was taken for three or four days. But after the prostration following the lumbar puncture had disappeared and when food and water were freely taken, there was no thirst, as before, and the amount of urine for a period of four weeks never exceeded 1800 c.c. for twenty-four hours. The specific gravity averaged 1015, ranging from 1005 to 1031 (single specimen). The result of the puncture suggests that the cause of the polyuria in this case was a lesion of the brain, perhaps in the hypothesis. This case also seems to indicate that, under certain conditions, the kidney of diabetes insipidus can, at least temporarily, pass a concentrated urine. Herrick gives a detailed history of the case in his article.



**Splenic Anemia Treated with Salvarsan.**—PERUSSIA (*Münch. med. Woch.*, 1912, lix, 1482) reports the case of a woman, aged thirty years, with very marked anemia, marked enlargement of both liver and spleen, edema, and suffering from persistent vomiting and diarrhea. The clinical picture was that of splenic anemia. The patient received three intravenous injections of 0.3 grams of salvarsan during a period of four weeks, and at the end of this time was apparently cured. Perussia does not know whether to attribute the good effects of the salvarsan to arsenic or to a possible spyhilitic basis for the trouble, or to a specific action of the salvarsan against the unknown cause of splenic anemia. VALLARDI (*Münch. med. Woch.*, 1912, lix, 1483) reports the case of a young man, aged twenty-two years, with very marked anemia and enlarged spleen. In this patient there was the history of a malarial attack lasting three months about one and one-half years before coming under Vallardi's observation. Operation was contraindicated by the enormous size of the spleen and a tendency to hemorrhage, and also by the poor general condition of the patient. He was given three intravenous injections of salvarsan (0.15, 0.4, and 0.4 gram), and an apparent cure resulted.

**A Preliminary Report on Neosalvarsan, with Particular Reference to its Employment as an Intramuscular Injection.**—WOLBARST (*Medical Record*, 1912, lxxxii, 145) gives the results of his clinical experience with Ehrlich's neosalvarsan. He believes that its effects are at least as striking as those of salvarsan. The reaction after treatment is slight with correct technique. Larger doses are better tolerated than is the case with salvarsan. The neutral reaction of the solution in water obviates the use of sodium hydrate, thus avoiding the possibility of thrombosis. Leakage of neosalvarsan solution into the tissues seems to be absorbed much more quickly than salvarsan. Neosalvarsan has no apparent effect on the eyes, kidneys, heart, or lungs. Intravenous injections of neosalvarsan may be repeated in two or four days. The neutral reaction of neosalvarsan solution lends itself readily to intramuscular injection. Wolbarst advises for intramuscular injection a suspension of neosalvarsan in glycerin. Neosalvarsan powder is mixed in a mortar with 3 to 4 c.c. of glycerin; to this is added a few drops of a 1 per cent. beta-eucain or alypin solution in distilled water. The suspension has now been converted into an almost clear solution. The buttocks are painted with iodine and four spots are located into which 1 c.c. of the solution is injected. Most patients have felt practically no pain; some have felt pain on sitting or standing for a day or two. The induration caused by the injection is very slight.

**The Influence of Theophyllin on Nitrogenous Excretion.**—FARR and WELKER (*Arch. Int. Med.*, 1912, x, 23) studied the changes produced by theophyllin on the urinary nitrogen in healthy persons and in nephritics. Most clinicians consider that theophyllin is contraindicated in acute nephritis, and of doubtful utility in chronic nephritis. It is generally agreed that theophyllin meets its best indications in the passive congestion and edema of heart disease, especially when combined with digitalis. Farr and Welker found that theophyllin

promoted the excretion of fluid in 2 cases but apparently did not affect, or even slightly diminish the excretion of nitrogen. In a case of diffuse nephritis diuresis failed to develop and the nitrogen elimination was sharply reduced. In a case of chronic interstitial nephritis the urinary partition was apparently changed by the drug so that it approached more nearly the normal. This may have been due to natural causes incident to convalescence. The slight or doubtful influence of theophyllin on nitrogen excretion and its pronounced influence on the excretion of water and sodium chloride suggests to Farr and Welker that this substance may act principally on the capsule of Bowman and little if at all on the tubules. Its failure to act in a given case might then be attributed to extensive involvement of the glomeruli.

---

**The Treatment of Syphilitic Diseases of the Nervous System by Salvarsan.**—COLLINS and ARMOUR (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1918) record the results of eighteen months' experience, during which time 75 patients suffering from syphilitic nervous disease were treated with salvarsan. They believe that the salvarsan treatment is effective but that in order to exert its best results, large doses must be given and frequently repeated. Of 36 cases of tabes in various stages of the disease, 22 showed striking, and in some instances, remarkable improvement both subjective and objective. In nearly every instance there was a decided increase of weight and a subjective feeling of improvement. The pain was lessened or relieved in many instances, and in the majority of cases, the ataxia was very much improved. In 2 cases, the pupils regained their capacity to react to light. Many of these patients had been under observation and treatment for many years, and the results obtained by salvarsan therapy were incomparably better than those obtained by mercury. They did not supplement the salvarsan treatment in these cases by the use of mercury, and did not give iodide of potassium, for they have long believed that iodide of potassium is injurious rather than beneficial in the treatment of tabes. Salvarsan was given systematically in 9 cases diagnosticated as general paresis. In 2 of these it was difficult to say whether the diagnosis should be tabes or paresis. It was in these 2 cases and in 1 undoubted case of paresis that great improvement took place. The improvement in the undoubted case of paresis seemed to be much more marked than the spontaneous remissions often occurring in the course of paresis. The most gratifying response to treatment was observed in the cases diagnosticated meningitis and meningomyelitis. In only 2 out of 6 cases of cerebral endarteritis of luetic origin was any perceptible improvement observed. Collins and Armour give details of a number of cases to illustrate the marked benefits derived from the salvarsan treatment of diseases of the nervous system of either direct or remote syphilitic origin. They are convinced that salvarsan is far more effectual than mercury for such cases.

---

**Five Years' Experience with the High Calory Diet in Typhoid Fever.**—COLEMAN (*Jour. Amer. Med. Assoc.*, 1912, lix, 363) has advocated that typhoid fever patients be fed on a more liberal diet on the ground that the requirements of the patient during the

febrile period are very inadequately met by a milk diet that has a caloric value of from 1000 to 2000 units. Coleman thinks that they require from 3000 to 5000 units. The number of foods originally employed was limited. With added experience the number has been increased until now the diet furnishes considerable variety. Coleman gives a table of appropriate foods with their approximate caloric values in his article. He believes that the foods most likely to prove harmful are meat and its preparations (except small quantities of meat broth, given for the purpose of stimulating the appetite and for sake of variety), vegetable foods containing much cellulose, and fruits containing much cellulose and small seeds, such as berries. Coleman answers some objections brought against the diet. It is claimed that patients cannot digest and absorb the amount of food recommended. He does not believe that typhoid fever causes severe impairment of the digestive powers. While there can be no doubt that food may cause disorders of digestion in typhoid, their occurrence depends not so much on the quantity as on the method of giving it. Sudden alterations in the diet, especially from a sparse to a rich diet, are likely to cause digestive disorders. Coleman believes that the majority of patients may be given the larger amounts of food not only without causing disturbances of digestion, but with the disappearance of previous indigestion. In regard to the capacity of the patient to absorb the larger amounts, investigations showed that the absorption of carbohydrate was practically complete, less than 0.5 per cent. being lost. The average loss of protein was 7.1 per cent. The average loss of fat in the active period of the disease, when the patients were taking from 147 to 200 grams, was 7.2 per cent.; in the steep-curve period and in convalescence, when the patients were taking from 150 to 258 grams, it was 4.5 per cent. The normal loss for similar diets is 3 per cent., but, according to Rubner, the loss of fat may reach 7.1 per cent. in health. The objection that the amount of fat recommended would inevitably cause alimentary disorders and acidosis has likewise been proved to be without foundation. Coleman answers the objection that, granting its absorption, patients do not require the amount of food which is advocated, by stating that patients lose both nitrogen and weight if they do not receive it. As measured experimentally, the high calory diet furnishes from 1000 to 2000 more calories than are expended by the patient in twenty-four hours, but the clinical evidence is convincing, according to Coleman, that they require the excess. In comparing the results obtained by the high calory diet with those obtained under the ordinary diets, the mortality percentage was 8.7 per cent. in the high calory cases, as compared with 16 per cent. in the other group. Convalescence seemed to be distinctly shortened and the symptoms of toxemia disappeared as a result of giving sufficient food.

---

**New Points of View in the Treatment of Diphtheria, Scarlet Fever, and Suppurative Processes.**—LOREY (*Med. Klinik*, 1912, viii, 1069) says that the therapeutic action of antitoxin in the treatment of diphtheria that has prevailed at Hamburg in epidemic form during the last three years has been disappointing. He advances the question whether it might not be feasible to secure an antitoxin derived from a

local strain of diphtheria bacilli. He suggests that a strain of bacilli might be found that has a more marked action in inducing paralysis, and an antitoxin derived from this strain might be more effectual for the severer forms of diphtheria. Lorey has had good results with the local application of antitoxin to the eye, nose, or throat in diphtheria or scarlet fever. The antitoxin is diluted with physiological salt solution and applied locally on compresses when possible, or used in the form of a spray or gargle. The membranes break up and are thrown off, while there is a profuse watery secretion underneath. This action is not due to the antitoxin content, and similar effects are noted when fresh horse serum is used. The same local treatment has been equally effectual in the sore throat of scarlet fever and in various suppurative processes.

---

**The Use of Hexamethylenamin in the Affections of the Upper Respiratory Tract.**—ESENBERG (*Jour. Amer. Med. Assoc.*, 1912; lviii, 2032) has used this drug in 43 cases, of which 22 were cases of acute bronchitis, 12 of acute rhinitis, 8 of influenza, and 1 of chronic sinusitis. It was given as follows: Children aged ten years received 4 gr. (0.3 gram) dissolved in one-half glass of water, three times a day during the first day, and twice a day during the following day or two. Children aged fifteen years received 6 gr. (0.4 gram) dissolved in a full glass of water, while adults received 10 gr. (0.7 gram) given in the same way. Cases of rhinitis were cured in from three to four days. In acute bronchitis every patient was well in four or five days, while influenza patients recovered in from five to seven days. No untoward symptoms were observed even when given in fairly large doses. This treatment seemed to prevent complications of acute rhinitis, such as bronchitis and sinusitis.

---

**The Rapid Cure of Amebic Dysentery and Hepatitis by Hypodermic Injections of Soluble Salts of Emetine.**—ROGERS (*British Med. Jour.*, June 22, 1912, p. 1424) says that the principal objection to the ipecac treatment of amebic dysentery is the production of very disagreeable and exhausting nausea and vomiting by the large doses that are essential to obtain its curative effects. This drawback is only imperfectly overcome by giving the drug in salol or keratin coated capsules, and the use of opium, chloral hydrate, or tannic acid to check vomiting. Vedder has shown that emetine, the principal alkaloid of ipecac, has the power in high dilutions of destroying amebæ in broth cultures, although it is not clear that this was a pathogenic form, which most recent authorities believe has not yet been cultivated. Rogers has, therefore, tested the effects of the soluble emetine hydrochloride on *ameba histolytica* in dysenteric stools. He found that, on placing a piece of mucus containing numerous active amebæ in normal saline solutions of this salt, the pathogenic organism is immediately killed and materially altered in its microscopical appearances by a 1 in 10,000 solution, while after a few minutes they are rendered inactive, and apparently killed by as weak a solution as 1 in 100,000. He therefore decided to try if this powerful alkaline can be safely administered hypodermically in the treatment of amebic disease, and obtained striking results in a few patients.

## O B S T E T R I C S

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

**Fatal Cases following the Early Getting up in Parturient and Operative Cases.**—AICHEL (*Zentralblatt f. Gynäkologie*, 1911, No. 6) reviews Frommé's case of embolism in a primipara, aged nineteen years, who got up on the second day for one hour in the puerperal period. Autopsy showed complete closure of the pulmonary vessels from an embolus the thickness of a finger, and thrombosis of the pelvic veins. In the thrombi were found streptococci. Scherer's case was that of a patient who aborted at three months, and was curetted to remove the remains of the placenta. On the third day the patient sat up for half an hour. On the fourth day fever developed, with continued high temperature, until the patient's death on the sixtieth day. From the second week the patient had daily chills. On the seventeenth day there was pain in the left lower extremity; on the twenty-sixth day the femoral vein became tender; on the thirty-second day the patient had cough; on the forty-second day bloody sputum; and on the forty-fourth day left-sided pneumonia. The patient died suddenly on the sixtieth day. At autopsy, there was thrombosis of the veins of the pelvis, the hypogastric veins, the left common iliac, vena cava, and femoral; purulent parametritis, and pelvic peritonitis. There were metastatic abscesses in the lungs, and pleurisy. In analyzing these findings, Aichel comes to the conclusion that they give no positive evidence that the getting up of the patient was the cause of the fatal issue. Infection and thrombosis develop in patients who remain in bed the usual time.

**The Technique of Suprasymphyseal Cesarean Section.**—FRANK (*Zentralblatt f. Gynäkologie*, 1911, No. 6) has changed somewhat his method in suprasymphyseal section, and in his last 5 cases, where the cervix was completely dilated at the time of operation, he has closed the uterus and abdominal wound, and allowed the placenta to be delivered through the cervix and vagina. He believes this to be a distinct improvement in the performance of the operation. His reason for adopting this change lay in the fact that in cases where he had expressed the placenta through the wound there had often been severe hemorrhage.

**The Development of Placenta Prævia.**—JOLLY (*Archiv f. Gynäkologie*, 1911, Band xciii, Heft 1) contributes a paper based upon cases examined in Bumm's clinic in Berlin, where in three different patients the opportunity was afforded to study the development of placenta prævia. He finds that placenta prævia develops only when the ovum has its preliminary attachment in the lower portion of the

uterine cavity. The insertion of the ovum and its development seems to depend largely upon the place of impregnation. There was a distinct interval between impregnation and the permanent attachment of the ripe ovum. The nearer to the uterus in the tube impregnation occurs, the greater is the movement of the ovum in the uterus before it becomes permanently attached. Different conditions of the mucous membrane of the uterus have an influence upon the insertion of the ovum. Endometritis undoubtedly causes the death of many impregnated ova; while in other cases the ovum becomes attached to the lower portion of the uterus, which may be free from pathological lesions. Uterine myomas are often the indirect cause, through their accompanying endometritis, of placenta prævia. Above the internal os the placenta develops in the decidua capsularis, which forms the external envelope at its deepest portion, covering the os uteri, and becoming the lower portion of the placenta prævia. The nourishment of this portion of the placenta is obtained through the decidua, whose vessels obtain blood from the sinuses of the uterus. Adhesions between the capsular decidua and the decidua vera rarely occur at the opening of the Fallopian tubes, and also at the internal os. Should such union develop, it is easily separated by slight hemorrhage. The placenta does not firmly adhere at the internal os because of its development in the decidua. In the early months of gestation placenta prævia may give the symptoms of carcinoma of the body of the uterus. The low attachment of the ovum and placenta prævia frequently cause interruption of the pregnancy. Many spontaneous abortions arise from placenta prævia. The bleeding in these cases is caused by the separation of the capsular decidua from the decidua vera through dilatation of the os, which opens vessels in the capsular decidua which are in communication with the placental site. Later, partial separation of the placenta follows, or laceration of the placental tissue. The indications for treatment are to compress the bleeding vessels at the site of the placenta and dilate the cervix. In extreme cases total extirpation of the uterus by abdominal section may be indicated.

---

**Induction of Labor with the Modified De Ribes Bag.**—BRODHEAD (*Amer. Jour. Obstetrics*, May, 1912) reports 139 cases of induced labor, 75 being private patients and 64 hospital cases. The method of introducing the bag is as follows: The usual preparations having been made, a 1 per cent. lysol vaginal douche is given, and the cervix dilated with the finger and with a steel dilator sufficiently to permit the introduction of one of the bags. The bag is twisted, the base of the bag pulled out, and the bag rolled up and carefully passed by forceps into the cervix, either by inspection or vaginal touch, and slowly filled with a sterile solution of lysol or salt. For this purpose the writer has devised a glass syringe with a rubber plunger which can be readily sterilized. The ordinary Davidson syringe may be used. When the bag has been completely filled the stem is clamped and tied. As a rule no traction is made, unless dilatation must be rapid, when traction is made at intervals of ten or fifteen minutes. When the first bag is expelled through the cervix, if labor has not begun, a larger one is introduced. This is usually followed in a few hours by the beginning of active labor. Where the cervix is almost completely dilated

by the bags without setting up active pains, the membranes may be ruptured, and if necessary delivery completed by forceps or version. Bags No. 2 and 3 were used in 73 per cent. of cases. In 41 cases labor was induced for contracted pelvis; in 27 for toxemia; in 19 for a large child; in 15 for overdue pregnancy; in 13 because the patient was at term and anxious to get through; and in 11 for a previous history of uterine inertia with instrumental delivery; in 4 cases the membranes had ruptured without labor developing; the other cases were induced for unusual conditions. In 6 cases, or 3 per cent., the membranes were accidentally ruptured during the insertion of the bags; in 3 cases, or 10 per cent., labor failed to develop with the use of the bags. In 85 per cent. of the primiparæ who were private patients, the introduction of not more than two bags was sufficient to bring on labor. In 2 patients where the bags failed to cause pains, they softened the cervix, and when the membranes were ruptured labor developed. In 42 multiparæ who were private patients, more than one-half were delivered by the use of one bag only; about one-third required the use of two. In 4 multiparæ, or 9 per cent., the bags failed to produce labor. In approximately 83 per cent. of multiparæ who were private patients, labor was induced by the use of not more than two bags. In cases where the bags failed to induce labor the patients were delivered by version or forceps, and in these cases the bags softened and dilated the cervix. An anesthetic was necessary for inserting the bags in one-sixth of the cases. In private primiparous patients labor began at once in 45 per cent., within twelve hours in 73 per cent., and within thirty hours in 79 per cent. With the private multiparæ, labor immediately began in 22 per cent., within twelve hours in 63 per cent., within thirty hours in 85 per cent. If both private and hospital primiparæ are considered, labor began at once in 49 per cent., within twelve hours in 76 per cent., within thirty hours in 85 per cent. With the multiparæ, immediate labor followed in 31 per cent., within twelve hours in 68 per cent., within thirty hours in 89 per cent. If all cases together are considered, immediate labor followed in 37 per cent., within twelve hours in 70 per cent., within thirty hours in 88 per cent. In all the primiparous patients, on an average eight hours and twenty-two minutes elapsed before labor developed; in all multiparous patients, ten hours and twenty-two minutes. The average for all patients was nine hours and forty-one minutes. The length of the induced labor averaged in primiparæ twenty-two hours and nine minutes; in multiparæ fifteen hours and fifty-two minutes; or in all, eighteen hours and two minutes. In all these cases 49 per cent. had normal labor, 21 per cent. low forceps, 11 per cent. medium forceps, 3 per cent. high forceps, 10 per cent. version, 3 per cent. breech extraction, 1 per cent. craniotomy, 1 per cent. Cesarean section, and 1 per cent. died without delivery. Among the 139 cases the use of the bags changed the presentation in 7, or 5 per cent. In only one of these cases was the outcome of the labor changed because of the use of the bag. Presentation or prolapse of the cord occurred in 6, or 4.3 per cent. In one case the bag slipped above the head, but labor developed and proceeded normally, and the bag was readily removed. There was practically no morbidity among the private patients, and but trifling morbidity among the hospital patients. The patient who died undelivered perished from eclampsia.

## GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

**X-ray Treatment of Gynecological Skin Affections.**—RUNGE (*Münch. med. Woch.*, 1912, lix, 1597) reports having treated 7 cases of severe idiopathic pruritis vulvæ with the x-rays, with complete success. There were no cases in which diabetes, or a leucorrhœal discharge, was present. In 5 of the patients complete cessation of itching occurred after one to three treatments; 2 others required a few more treatments, but in these also a complete cure was eventually attained. Runge has had like favorable results in the treatment of 2 cases of severe eczema of the vulva due to an irritating vaginal discharge; the discharge was treated simultaneously by the usual methods, but Runge attributes the cure of the eczema to the x-rays, as the discharge had been treated for some time previous to beginning the use of the rays, with no apparent benefit to the skin condition. In 1 case of advanced kraurosis, practical disappearance of the itching was brought about by x-ray treatment, but no other effect could be observed. In the treatment of these conditions Runge uses a tube somewhat harder than those usually employed for dermatologic purposes. Since we do not know whether the seat of the trouble in pruritis and allied affections is purely superficial or somewhat deeper, he considers it advisable to use a tube which, in addition to the rays of superficial action, gives off some of a moderate degree of penetrating power. An exposure amounting to just short of an erythema-dose is given, either at one sitting, or divided between two successive days, and an interval of two to three weeks then allowed to elapse before the next treatment.

**Constipation and Headache in Women.**—In an article bearing the above title, REED (*Jour. Amer. Med. Assoc.*, 1912, lix, 354) expresses the belief that in many patients presenting the very common symptom-complex of constipation, headache, painful menstruation, tender ovaries, with more or less displacement of the uterus, the real source of the trouble lies in a displaced stomach and colon. Such patients are usually treated gynecologically solely on the assumption that the constipation may be due to the pressure of a retro-displaced uterus on the rectum, that the headaches are of reflex origin from the genital organs, and so forth. In many of these women, however, gynecological treatments or operative procedures produce no relief from the constant headaches; in such cases a careful x-ray will generally show a condition of gastrocloptosis to be at the bottom of the trouble, and not until this is properly corrected do the symptoms, resulting largely from the absorption of toxins, disappear. While not for a moment denying the importance of correcting any marked displacements of the uterus



which may be present, nor assuming that every case in which some ptosis of the stomach and colon is present is necessarily accompanied by the above mentioned symptoms, Reed emphasizes that where such demonstrable lesions are present, associated with these symptoms, the gastro-intestinal condition will generally be found to be of far greater etiological importance than the gynecological.

**Relative Value of Various Substances Used as Douches.**—A systematic test of a number of the commoner substances used as ingredients of vaginal douches has been made by POLANO (*Zeitschr. f. Geb. u. Gyn.*, 1912, lxx, 394), in order to determine their relative effect on the chemical reaction and bacterial content of the vagina. For this purpose each substance has, as a rule, been tried on three dispensary patients, some of whom showed clinically symptoms of inflammation of the vagina, others of whom did not. The method of making the examination was briefly as follows: A tri-valve speculum was introduced and the valves spread apart. A platinum loopful of secretion was then taken from the right side of the vagina near the introitus, one from the left side, and one from each vaginal vault. From these, cover-slip smears were made, and examined microscopically. Four similar loopfuls were inoculated on agar plates and cultured. The speculum was then removed, and 1 liter of water containing the substance to be tested given as a douche to the still recumbent patient. This process was repeated in each case on three successive days. In many instances there was a marked lack of correspondence between the appearance of the smears and the cultures, the plates often showing almost complete absence of growth after treatment, while the smears apparently contained as many organisms as before. Polano believes the explanation of this to be that many of the organisms become temporarily reduced in virulence by the treatment, and while still being present, do not possess enough vitality to grow well. He has not found any permanent effect to be produced on the chemical reaction of the vagina, nor any change in the character of the bacterial flora to be brought about by any of the substances tested, though a quantitative diminution in the bacteria present could in many cases be demonstrated. The most effective substances in this respect were found to be alum, alcohol, alsol, silver nitrate, and bolus alba. Less satisfactory, but still of some value, were lysoform and iodine, while pyroligneous acid, lysol, and lactic acid gave the poorest results. It is evident, Polano concludes, that dessicating and astringent properties are of much greater importance in substances to be used as douches than bactericidal power or acidity.

**Control of Hemorrhage in the Radical Operation for Carcinoma Uteri.**—One of the most important factors in producing the very high primary mortality of the so-called "extended" or Wertheim operation for carcinoma of the cervix (averaging in most statistics about 20 per cent.) is conceded by most authors to be hemorrhage—not so much arterial bleeding, as venous oozing from the deep pelvic veins, which it is at times very difficult to control. PETERSON (*Surg., Gyn., and Obstet.*, 1912, xv, 135) has found this to occur chiefly in three places: (1) From the transverse vesical veins which run across the ureter,

(2) from the veins which lie close to the uterus and the ureter, and (3) from the veins posterior to the uterus lying in close connection with the rectum. In his experience hemorrhage from the last source is, as a rule, easily controlled; that from the vesical veins is best managed by separating the bladder from the vagina and uterus in the median line only, never trying to separate it at the sides until after the vesical veins have been secured by forceps on each side of the ureter. They may then be tied, cut, and the ureter dissected out of its bed without danger. Bleeding from the remaining veins can usually be controlled by pushing the ureter away from and down into the pelvis, clamping always toward the uterus. In this way danger of injuring the ureter is avoided. FROMME (*Zeitsch. f. Geb. u. Gyn.*, 1912, lxxi, 321), in discussing the same subject, says that he has seen 2 cases in which severe hemorrhage came from large venous sinuses situated in the dense connective tissue so closely attached to the pelvic wall that no ligature could be applied. Packing was ineffectual, and the only way to stop the bleeding was to catch the vessels with long, thin artery forceps. Since it was impossible to replace these by ligatures, they were left in position, the handles protruding through a small opening at one end of the abdominal incision. The forceps were allowed to remain in place for forty-eight hours; both patients had an uneventful convalescence, but one had to be subsequently re-operated upon for a small recurrence. The same difficulty was again encountered, and the same procedure carried out, with equal success.

**Histology of Pyosalpinx.**—A very decided opinion as to the impossibility of distinguishing histologically between salpingitis of gonorrheal origin and that due to other forms of infection has been recently expressed by MILLER (*Monatsschr. f. Geb. u. Gyn.*, 1912, xxxvi, 211). As is well known, Schridde and other authors have advanced the hypothesis that gonococci produce very definite and specific changes in the tube, which are not produced by other bacterial invaders, these changes consisting chiefly in a thickening of the mucous folds, with loss of surface epithelium, and the formation of adhesions between adjacent folds, but more especially in an infiltration of the folds by masses of plasma cells, lymphocytes, and lymphoblasts. The most important elements of all he considers to be the plasma cells, from the presence of which in any considerable numbers, in the tissue or in the free exudate, "a positive diagnosis of gonorrhea is justifiable." Miller, however, maintains that theoretically it is very difficult to understand why plasma cells should possess a specificity in the tube which they do not show in any other part of the body. They are found, as has been repeatedly shown by various authors, in many forms of inflammatory granulation tissue, in infectious granulomas, in the primary lesions of syphilis, and in the brain in various conditions, such as lues cerebri, dementia paralytica, acute alcohol and phosphorus poisoning, idiocy, sleeping sickness, etc. Miller does not rest his objection to Schridde's teaching on theoretical grounds alone, however. He has found in several cases of tuberculous pyosalpinx large numbers of plasma cells present, reaching to as high as 25 per cent. of the elements composing the free exudate in the lumen. In numerous cases of streptococcic tubal infection *post abortem*, in which there were no

grounds for suspecting the presence at any time of a gonorrheal infection, and in several of unilateral pyosalpinx following appendiceal abscess, in which gonorrhea could be positively excluded, he found plasma cells in large numbers, and all the other histological features considered by Schridde to be characteristic for gonorrhea. He concludes, therefore, that these criteria are all worthless, and that we do not possess at the present time any means of distinguishing with certainty between tubal infections due to the gonococcus and those due to the streptococcus or staphylococcus, except in the comparatively small group of cases in which it is possible by staining or cultural methods to demonstrate directly the invading organism.

---

## HYGIENE AND PUBLIC HEALTH

---

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.,

AND

ARTHUR I. KENDALL, PH.D., DR.P.H.,

DEPARTMENT OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL.

---

**Infectious Abortion and its Relation to Man.**—THEOBALD SMITH and MARSHALL FABYAN (*Centralbl. f. Bakt., Orig.*, 1912, lxi, 549 to 555), MARSHALL FABYAN (*Jour. Med. Research*, July, 1912, xxvi, 441 to 487) EDWIN S. GOOD (*Kentucky Agr. Exp. Sta. Bull.*, p. 165), FRANK M. SURFACE (*Annual Report of the Kentucky Agr. Exp. Sta.*, 1912, pp. 303 to 366) and others have recently studied a disease of cows and mares known as infectious abortion, which appears to threaten man. The disease is little known to students of human medicine, and a brief review of its essential features is therefore given. It has been suspected for nearly a century among farmers and breeders of horses and cattle that abortion was contagious in many instances and might spread from animal to animal in a herd. Not until 1895, however, was this suspicion made definite. In that year the Danish veterinarian, Professor Bang, and his assistant, Stribolt, isolated a small bacillus from abortive cows which has been proved beyond all doubt to be the cause of infectious abortion among cattle. Owing to certain peculiarities in the method of growth of this bacillus, many of the best pathologists have failed, however, to find it for a long time. Recently, however, a number of investigators in this country and abroad have isolated the organism and subjected it to careful study both culturally and experimentally. There can be but little doubt that this organism causes a very large economic loss yearly in this country and abroad. Statistics are not available for the most part, but Wall showed that among herds in Denmark, where infectious abortion was known to be present, more than 93 per cent. of the abortions were due to this specific organ-

ism. Among herds where slips occur only rarely, that is to say, in herds apparently not infected, he found that 27 per cent. of the abortions were in all probability due to this infectious disease. Similarly, Zwick, in Germany, has also called attention to the fact that this disease is far more widely spread there than is generally recognized.

**CLASSIFICATION OF ABORTION IN LIVE STOCK.**—WILLIAMS, writing on veterinary obstetrics, recognizes three distinct classes of abortion in domestic animals: (1) Sporadic or accidental abortion; (2) enzoötic abortion due to some infectious disease of the mother, such as tuberculosis, which brings about the death and expulsion of the fetus as a complication of the maternal disease; and (3) infectious abortion, an infection of the fetus and its membranes, which causes the death and expulsion of the fetus or its expiration in the living and febrile state at any period of gestation from the date of conception to the normal conclusion of pregnancy without directly introducing material evidence of disease in the mother.

**MANNER OF INFECTION.**—It was originally believed that infection was transmitted through the bull, but recent investigations seem to show very definitely that the main channels of infection are through the vagina and also through the alimentary canal by ingestion. These investigators believe that infection may reach the uterus even before pregnancy, setting up in the uterus an inflammatory process between the fetal and maternal membranes, resulting in a purulent exudate which causes a partial separation of these membranes and the premature delivery of the fetus. Investigations also indicate that the organism is able at times to actually enter the circulation of the fetus through the medium of the placenta to the blood stream.

**SYMPTOMS.**—MCFADYEAN and STOCKMAN, of the English Abortion Committee, found that animals experimentally infected with the disease occasionally exhibit a slight rise in temperature after infectious material was given. This is not always the case, however, and they decided that "under natural conditions infection is insidious and usually no noticeable symptoms arise until the animal is about to abort."

**THE MORPHOLOGY AND CULTURAL CHARACTERS OF B. ABORTUS.**—The organism is from 0.5 to 0.6 microns in diameter and from 0.6 to 3 microns long. There may be some variation in the length. The diameter is fairly constant. The organisms ordinarily lie separately or in pairs, very rarely in chains. There is no motility although Brownian movement may be very pronounced. The bacillus stains readily with all ordinary dyes, staining uniformly, as a rule, although occasionally certain irregularities in staining may be noticed. The organism is Gram negative; no capsules, flagella or spores have been demonstrated. In old cultures, degenerated and involution forms may be seen and rarely branched forms. On agar colonies appear as rather small transparent growths resembling dewdrops. Later they assume a yellowish-brown color. Growth on gelatin is very slow, probably because of the low temperature (20°) at which gelatin is incubated. After a week or ten days; however, small colorless colonies usually appear. No liquefaction of gelatin takes place. On the agar-gelatin serum medium of Bang a growth occurs either at the surface or in a zone sharply circumscribed and immediately below the surface.

In ordinary broth a slight clouding usually appears after forty-eight hours, which gradually becomes rather dense, and then after a variable period tends to clear up. As a rule, no pellicle forms on the surface even after long incubation. The organism grows fairly readily in milk without, however, producing any acid. In fact a slight but definite amount of alkali is produced in this medium. The optimum temperature for growth is  $37^{\circ}$  C. The organism grows very slowly at  $20^{\circ}$  C. According to Preisz, the organism withstands exposure to  $50^{\circ}$  C. for thirty minutes, but is killed at  $55^{\circ}$  C. usually within ten minutes.

**THE DIAGNOSIS.**—MCFADYEAN and STOCKMAN have attempted to diagnosticate infectious abortion by means of a substance which they call "abortin." This substance is prepared in precisely the same manner as is mallein. The results although interesting are not wholly satisfactory. A much more satisfactory procedure appears to be the well known deviation of complement method which is carried out in the usual manner. Fabyan has studied the pathogenesis of *B. abortus* in guinea-pigs and finds that although the disease in cows is apparently a rather strictly limited one, in guinea-pigs the organism produces a marked general infection. Generally speaking the most characteristic feature of the guinea-pig disease is a greatly enlarged spleen showing large edematous areas of degeneration and a swollen liver with numerous necrotic areas. Similarly Schoreder has studied the same disease and has noted the same general phenomena at autopsy, and has called attention to the fact that the lesions may resemble, in a general way, those of tuberculosis. He has made an interesting observation that in the males very frequently there is a more or less complete breaking down of the testicles. In rare instances there may be paralysis and a peculiar type of joint disease. It is a very significant fact that in a few instances women who give a history of abortion show, by the deviation of complement method, the presence of *B. abortus*. Realizing that this organism may occur, and apparently does occur in milk, the significance of these discoveries cannot be overlooked. Fortunately heating milk to the temperature of  $60^{\circ}$  C. for a few minutes will certainly remove this danger. From the hygienic point of view this disease which hitherto has not received the attention which it deserves, is an entity which must be taken into consideration not only with respect to the dairy industry, but also must be regarded as a probable invader of man.

---

**Alimentary Anaphylaxis.**—O. H. RICHET (*Compt. Rend. Soc. Biol.*, 1911, i, 44) has thrown additional light upon the interesting occurrence of acute symptoms caused by various substances such as shellfish, strawberries, and sometimes by standard articles of diet such as eggs, veal, oatmeal, etc. In the light of our present knowledge it appears that these disturbances are instances of local hyper-susceptibility, and that the acute poisoning is brought about by the sharp muscular and vascular reactions which take place in the sensitized intestinal mucosa upon ingestion of the particular substance in question. Richet gave 0.37 gram per kilo of kreptin to a dog by the mouth, and four weeks later 0.14 gram per kilo also by the mouth. This produced mild indications of anaphylaxis. Two days later the dog was refractory to an intravenous injection while a control dog similarly treated, but

which did not have the second feeding by the mouth, promptly died in anaphylactic shock. Richet also found that when krebitin is given by the mouth the sensitized animals showed a marked leukocytosis at the second feeding. If the animal survived the anaphylactic shock the late symptoms of poisoning due to the krebitins did not appear, therefore they were rendered immune.

---

## PATHOLOGY AND BACTERIOLOGY

---

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME  
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT;  
SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

---

**The Influence of Local Anemia upon the Action of Poisons and upon Infective Processes.**—R. BESTELMEYER (*Br. Beitr.*, 1912, Band lxxviii, Heft 2, S. 333) notes, as a result of his experiments, some interesting facts. Although there is no actual killing of virulent bacilli by reason of a locally produced anemia, yet the resorption of injected soluble poisons is so retarded that ordinarily fatal doses may be injected without producing a fatal effect. This was proved by the use of various snake poisons. With the slowing of the capillary current there is a corresponding lowering of the rate of absorption; with a quickened capillary current more poison is absorbed. In infective states, local anemia delays the entrance to the blood stream of bacteria and their toxins. The general and local manifestations appear later, but there is a greater tendency to localized necrosis, although secondary abscesses by way of the lymphatics are less prone to occur. Passive hyperemia, Bestelmeyer points out, is anemia, as far as the arterial blood is concerned.

**Vaccination with Sensitized Agents.**—BESREDKA (*Bull. d. l'Inst. Pasteur*, June 30, tome x, No. 12) deals anew with the question of vaccination by means of agents, living or dead, that have been attenuated in various ways. In the case of tubercle bacilli, if attenuated, sensitized bacilli are used, they are not only themselves absorbed more quickly than ordinary bacilli, but they in some way hasten the absorption of bacilli injected subsequently to their own entry into the body. The sensitized bacilli (if one may so translate *sensibilisés*) are better borne by the animal than are the non-sensitized, to the extent that with the former, repeated injections do not kill; as to the power as a vaccine, guinea-pigs treated with sensitized bacteria contracted disease from subsequent inoculation with ordinary virus, but after long delay and of light grade of severity. Meyer used the sensitized vaccine on 47 persons; localized tuberculosis, such as abscess or fistula, healed rapidly, while bone and joint lesions were quickly bettered; 40 out of 47 cases showed definite amelioration. Vallée and Guinardre report equally good results in 30 women; all these observers unite in declaring

the innocuousness of the sensitized bacteria. With reference to sensitized pneumococci as a vaccine, Leon and Aoki have had good results in experimental animals; the innocuity is quickly obtained and is more durable than in the case of ordinary pneumococci. A negative phase is not obtained after injection, and the immunity to subsequent inoculation was sometimes very striking. Vaccination against typhoid fever is of interest in view of the fact that Besredka (with Metchnikoff) has used the living sensitized typhoid bacilli for the purpose. Encouraged by the results obtained in chimpanzees, they have carried on the experiments in man. Alcock has proved in the case of 44 persons that the procedure is a harmless one; the sensitized vaccine leads to little or no general or local reaction, and Besredka states that 700 human subjects of recent experiments bear witness to its harmlessness. He cites the work of Garbat and Meyer, as to the effect on the serum of the inoculated animals. The immunity of these animals surpassed that of the animals immunized in the old way, nevertheless, neither agglutination nor fixation of the alexin could be cited as indications of this immunity.

---

**Some Facts about the Epidemiology of Tuberculosis.**—A. CALMETTE (*Ann. de l'Inst. Pasteur*, July, 1912, vol. xxvi) has brought forward considerable evidence upon the existence of tuberculosis in the French colonies. In the tropics, tuberculosis goes hand in hand with civilization. Black races, where they are uncontaminated from without, remain very free from the disease. None, however, of the races studied were immune, and the last comers to civilization were less immune than those who had mixed somewhat with the outside world. "It is no longer possible," says Calmette, "to support the hypothesis formulated by von Behring in 1903 that pulmonary tuberculosis in the adult is only a late manifestation of an infection of bovine origin, contracted in the earliest months of life as a result of the ingestion of milk from a bacilli-carrying cow." Among the indigenous population of West Africa and Indo-China, infants are found free of infection up to the time of weaning, after which they are subject to familial and other infections, especially by the custom prevailing in Indo-China, by which some older person chews the rice before putting it into the child's mouth. Later, the pipe, the betel, or the kola nut is freely transferred from mouth to mouth. In West Africa, Indo-China, the Antilles, and in Oceania, "interhuman" contamination alone is at work, since children drink no cow's milk, and indigenous cattle are as yet uninfected. In older colonies, the conditions approximate to the state of affairs seen in Europe, and tuberculous milk must be admitted to be in some degree responsible.

---

**The Process of Vital Staining.**—W. SCHULEMANN (*Zeitsch. f. exper. Path. u. Ther.*, 1912, Band xi, Heft. 2) makes certain observations upon the relationship between the chemical constitution of cells and their stainability during life. He considers that the granules in the cells that exhibit the stain are formed as a result of the entry of the coloring material to the cell, and that there occurs a chemical combination between the coloring matter and a (hypothetical) reaction-body which is formed for the purpose. This view is supported by the fact that in intensifying experiments where the color is re-administered, the

number of granules increases but not the intensity of color of the individual granule. The form of these granules is not constant, and seems to depend upon the speed of diffusion of the coloring agent, being smaller and more uniform with slowly diffusing agents, larger, more irregular, and even at times cubical with those agents that diffuse rapidly. Attempts at combined staining of the granules are unsuccessful, and the granules are entirely absent in certain types of cell, both of which facts are cited in favor of the existence of reaction-bodies; even stronger evidence is the observation that in a cell where poisons are present which damage the reaction-bodies, these become free and diffuse out of the cell. Goldmann considers the reaction-body to be a lightly-bound fat-albumin molecule or group of molecules.

**A Comparative Study of Antibodies.**—It is daily becoming better understood that all antibodies that are produced by the cell are not available for the cure or prevention of infection or disease; that the existence of one antibody in excess does not speak for the necessary existence of another. KOLMER (*Jour. of Med. Research*, July, 1912, vol. xxvi, No. 3) found, in typhoid and cholera immune serums, that there is no relation between the degree of complement fixation and the opsonins, agglutinins, and bacteriolysins, while there did appear to be a relation between the amount of opsonins and of bacteriolysins. The same antigen may stimulate the production of different antibodies, lysins, agglutinins, opsonins, antitoxins, and other complement-fixing bodies, and one antigen tends to produce excess of one or more antibodies, while another antigen produces others. Each antibody has a direct relationship to its antigen, but not necessarily to the other antibodies. Nevertheless, the existence of an excess of one or more of the antibodies is often good presumptive evidence of the existence of excess of yet others. The presence of complement fixation is not, however, such good evidence as it at first appeared, of the existence of protective antibodies. Kolmer found that the complement-fixing body (an antibody in one sense of the word) bore no relation to the other antibodies. In curative and prophylactic serums, it is true that the antitoxins, the bacteriolysins, and the opsonins bear some relation quantitatively one to another; but the agglutinins (and precipitins) are not directly opposed to the antigen, and are not definitely protective to the organism, although the serum which shows an excess of these probably contains excess of the other bodies which are protective. Complement fixation power, Kolmer concludes, is not a measure of bactericidal power; there is probably a special antibody produced which is capable of binding hemolytic complement without, at the same time, being protective to its own organism or destructive to the antigen which gave rise to its production.

---

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL*.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript*.

All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.



# CONTENTS

## ORIGINAL ARTICLES

<b>Tertiary Syphilis of the Liver</b> . . . . .	625
By THOMAS McCRAE, M.D., F.R.C.P. (Lond.), Professor of Medicine in the Jefferson Medical College, Philadelphia.	
<b>Maltose in Infant Feeding</b> . . . . .	640
By JOHN LOVETT MORSE, A.M., M.D., Associate Professor of Pedi- atrics, Harvard Medical School; Associate Visiting Physician at the Children's Hospital and at the Infants' Hospital, Boston.	
<b>Bismuth Poisoning</b> . . . . .	647
By LOUIS M. WARFIELD, M.D., Milwaukee, Wisconsin.	
<b>Weight Curves in Typhoid Fever</b> . . . . .	659
By WARREN COLEMAN, M.D., Professor of Clinical Medicine and Applied Pharmacology, Cornell University Medical College; Visiting Physician to Bellevue Hospital, New York City.	
<b>Observations upon Scarlet Fever, Diphtheria, and Measles at the Cin- cinnati Contagious Hospital</b> . . . . .	669
By ALBERT J. BELL, A.B., M.D., Visiting Staff, Contagious Group, Cincinnati Hospital.	
<b>Studies on the Motor Functions of the Stomach by the Use of the Gastric and Duodenal Fistulas, Especially as Regards the Influence of the Bitter Waters and Bitter Salts, that is, Those Containing Magnesium Sulphate or Sodium Sulphate</b> . . . . .	682
By THOMAS R. BROWN, M.D., Associate in Medicine, Johns Hopkins University, Baltimore, Maryland.	
<b>The More Common Forms of Cardiac Irregularity, with the Report of a Case of Heart-block</b> . . . . .	697
By THOMAS A. CLAYTOR, M.D., Clinical Professor of Medicine, George Washington University; Physician to Garfield Hospital and to the Tuberculosis Hospital, Washington, D. C.	
<b>Cryptogenetic Granulomatosis of the Stomach</b> . . . . .	707
By O. C. GRUNER, M.D., and E. J. MULLALY, M.D., Montreal, Canada.	
<b>The Alimentary Hypersecretion of Chronic Ulcer as Shown by the Lactose Test Meal</b> . . . . .	715
By DUDLEY ROBERTS, M.D., Attending Gastro-enterologist, Brooklyn Hospital; Consulting Gastro-enterologist, Coney Island Hospital and King's Park State Hospital, Brooklyn.	
<b>Intermittent Spinal Claudication</b> . . . . .	721
By FRANK F. D. RECKORD, M.D., Resident Physician in the Hospital of the University of Pennsylvania, Philadelphia.	

<b>The Metastasis of Hypernephroma in the Nervous System: Jacksonian Epilepsy Caused by Such Lesion</b> . . . . .	<b>726</b>
By JOSEPH COLLINS, M.D., Physician to the Neurological Institute of New York, and R. G. ARMOUR, M.D., Chief of Clinic to the Neurological Institute of New York.	
<b>Metabolic Observations on Amyotonia Congenita</b> . . . . .	<b>732</b>
By J. C. GITTINGS, M.D., and RALPH PEMBERTON, M.S., M.D., Philadelphia.	

---

## REVIEWS

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., C.B., D.Sc., LL.D., F.R.C.S., F.R.S., and F. F. Burghard, M.S. (Lond.), F.R.C.S. . . . .	739
Pellagra, an American Problem. By George M. Niles, M.D. . . . .	743
Clinical Disorders of the Heart Beat. By Thomas Lewis, M.D., D.Sc., M.R.C.P. . . . .	744
Delayed and Complicated Labor. By Robert Jardine . . . . .	745
Surgery of Deformities of the Face, Including Cleft Palate. By John B. Roberts, A.M., M.D. . . . .	746
Die Störungen des Farbensinnes ihre klinische Bedeutung und ihre Diagnose. Von Dr. Hans Köllner . . . . .	747
Diseases of Infants and Children. By Henry Knight Chapin, and Godfrey Roger Pisek . . . . .	748
Preventable Cancer. By Rollo Russell . . . . .	749
Gonococcus Infections. By Major C. E. Pollock, and Major L. W. Harrison . . . . .	750
Aids to Histology. By Alexander Goodall . . . . .	750

---

## PROGRESS OF MEDICAL SCIENCE

### MEDICINE

#### UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

On the Causation of Parenchymatous Nephritis . . . . .	751
On the Function of the Circle of Willis . . . . .	752
Experimental Studies on the Administration of Salvarsan by Mouth to Animals and Man . . . . .	752
"Floating" or Movable Kidney Considered from the Practitioner's Standpoint . . . . .	753
Tests of the Efficiency of Pasteurization of Milk under Practical Conditions . . . . .	753
A New Symptom of Aneurysm of the Aorta . . . . .	754
Röntgen Examination and Glycyl-tryptophan in the Diagnosis of Cancer of the Stomach . . . . .	754
A Simple Method for the Determination of Uric Acid in the Blood and in other Colloidal Fluids . . . . .	755

**SURGERY**

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

General Toxicity of Extracts of Hypertrophied Prostate . . . . .	756
Experimental Researches Concerning Ulcerations of Large Arteries from Contact with Drains . . . . .	756
Surgical Treatment of Genital Tuberculosis in the Male . . . . .	757
The After-treatment of Excision of the Knee with the Aid of Approxima- tion of the Bones by a Screw Splint . . . . .	757
After-treatment of Excision of the Knee . . . . .	758
The Technique and After-treatment of Excision of the Tuberculous Knee . . . . .	758
The Technique and After-treatment of Excision of the Knee . . . . .	759
Intravenous Administration of Sublimite, Hyrgolum, Oxycyanide, and Sublamine, in Salvarsan Relapses . . . . .	760
The Value of Direct Gastroduodenoscopy in Affections of the Stomach and the Duodenum . . . . .	761

**THERAPEUTICS**

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Luminal—A New Hypnotic . . . . .	761
The Action of Salvarsan and Neosalvarsan on the Wassermann Reaction . . . . .	762
Influence of Salvarsan Treatment on the Wassermann Reaction . . . . .	763
Lumbar Puncture in the Treatment of Uremia . . . . .	763
Clinical Experience with Luminal . . . . .	763
The Salvarsan Treatment of Pernicious Anemia . . . . .	764
The Treatment of Scarlet Fever with Salvarsan . . . . .	764

**PEDIATRICS**

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

Vaccines in the Treatment of Pertussis . . . . .	765
Intestinal Poisoning under the Guise of a Cerebral Affection . . . . .	765
Massage in Wasting Diseases of Children . . . . .	766
The Treatment of Asthma in Children . . . . .	766
Typhoid Fever in Infancy . . . . .	767

**OBSTETRICS**

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Uterine Scar After Cesarean Section . . . . .	768
Rupture of the Cranial Dura Mater in the Newborn . . . . .	768
Prognosis of Repeated Classic Cesarean Section . . . . .	769

Retroversion of the Gravid Uterus with Over-distention of the Bladder and Hematuria . . . . .	769
Cesarean Section for Dystocia, Due to Coils of the Cord around the Fetus . . . . .	770
Congenital Graves' Disease, and Total Occlusion of the Duodenum in the Newborn . . . . .	770

---

## GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Kidney Changes Following Sudden Occlusion of the Ureter . . . . .	771
Operation for Carcinoma of the Vulva . . . . .	773
Trauma as a Factor in Rupture of Pyosalpinx . . . . .	773

---

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.

Carcinoma of the Tongue Treated by Adrenalin . . . . .	774
Farcy (Glanders) of the Larynx and Pharynx . . . . .	774
Asphyxia from Descent of Excised Adenoids in the Trachea, Revealed by Bronchoscopic Intervention . . . . .	775
A New Method of Plastic Injections . . . . .	775
Radical and Aseptic Cure of Frontal Sinusitis by Plugging the Sinuses . . . . .	775
Nasal Stenoses . . . . .	775
A New Treatment for Paralysis of the Recurrent Nerve . . . . .	775
Facial Paralysis Following the Use of the Nasal Douche . . . . .	776
Laryngeal Paralysis as the First Symptom of a Cancer at the Base of the Skull . . . . .	776
Secondary Cancer of the Larynx . . . . .	776
Gastroscopy . . . . .	776

---

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.

Pneumococcus Infection in Man and Animals . . . . .	776
Hemoglobinemia and Hemoglobinuria . . . . .	777
Salvarsan and Sublimate . . . . .	778
The Distribution of Iodine in Normal and in Syphilitic Tissue . . . . .	778
The Parasitology of Trypanosomiasis . . . . .	779
The Disinfection of Drinking Water by Chlorinated Lime . . . . .	779
The Experimentally Alcoholic Heart and Liver . . . . .	780

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

NOVEMBER, 1912

---

ORIGINAL ARTICLES

TERTIARY SYPHILIS OF THE LIVER.<sup>1</sup>

By THOMAS McCRAE, M.D., F.R.C.P. (LOND.)

PROFESSOR OF MEDICINE IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

(From the Medical Clinic of the Johns Hopkins Hospital.)

THERE is a peculiar importance attached to the recognition of late syphilis in that diagnosis may mean and determine the issue between life and death. This is most strikingly shown in the tertiary lesions of the nervous system, but it also applies to syphilis of the liver. The symptoms caused by it are often serious and without diagnosis the issue may be fatal, whereas with its recognition and proper treatment we have in the majority of cases a demonstration of one of the most brilliant results of therapy. It is the recognition which is so important and therefore the clinical features are especially considered in this paper.

The study is based on 56 cases which were admitted to the medical service of the Johns Hopkins Hospital. The cases of early congenital syphilis are not included; they form a group well recognized and are not considered here. The cases regarded as late congenital syphilis are included.

The incidence of tertiary hepatic syphilis is difficult to state with any accuracy. These 56 cases occurred among 27,500 general medical cases, and it does not seem unlikely that an unknown number were overlooked. Among 3300 autopsies at the Johns Hopkins Hospital there were 46 of well marked syphilis of the liver,

<sup>1</sup> Read before the Association of American Physicians, May 14, 1912.  
VOL. 141, NO. 5.—NOVEMBER, 1912.

but in many of these there were no clinical manifestations. Rolleston<sup>2</sup> quotes 64 cases among 11,629 autopsies at St. George's Hospital, London, and Flexner<sup>3</sup> 88 cases among 5088 autopsies at the Philadelphia Hospital. It is probable that the condition is more common than is generally recognized.

*Etiology.* The essential etiological factor does not require discussion. The contributing factors were as follows:

*Age.* The distribution by decades was:

1 to 10	1
11 to 20	2
21 to 30	11
31 to 40	19
41 to 50	16
51 to 60	4
61 to 70	3

The 3 cases below the age of twenty years were regarded as instances of late congenital lues. The age of onset in these was three years, thirteen years, and sixteen years. The oldest patient in the series was aged seventy years.

*Color.* Of the series, 34 were white and 22 colored. This shows an unusually high percentage among the colored patients, the ratio being 1.8 to 1, whereas in the medical service of the hospital the figures are about 5 to 1.

*Sex.* This shows a preponderance of males, there being 41 males and 15 females. The number of colored females is striking, 10 out of the 15 females being colored. There were only 12 colored males. The explanation of the incidence in males may lie in the greater prevalence of syphilis, although this may not apply in the colored race, but it is of interest to inquire the effect of over-indulgence in alcohol.

*Alcohol.* The three patients below the age of twenty can be excluded. Of the cases in which there was a definite note as to alcohol, in only 4 was there no history of drinking. Of 37 with a definite history, in only 3 was the record of slight use; 19 described themselves as moderate users, and 14 had taken it to excess. This is rather striking and shows a very high percentage of moderate or heavy users of alcohol. It may be a factor in determining the occurrence of hepatic syphilis, not, however, meaning by this that syphilis is engrafted upon alcoholic cirrhosis.

*History of Syphilis.* In the 3 congenital cases, there was a positive history of syphilis in the father of one; in the other two the history was very suggestive, as both mothers had had several miscarriages. In the adults there was a definite history of a primary infection in 26. In 9 others' syphilis was suggested by a history of iritis, sore throat associated with eruption, miscarriages, etc. The time which had elapsed since the primary sore in the cases

<sup>2</sup> Diseases of the Liver, 1905.

<sup>3</sup> New York Med. Jour., 1902, p. 10.

with a positive history varied from four to twenty-five years. There were 3 cases with an interval of four years and 3 with five years. With an interval of from six to ten years inclusive there were 7 cases, from eleven to fifteen years 8 cases, from sixteen to twenty years 3 cases, and from twenty-one to twenty-five years 2 cases.

*Morbid Anatomy.* There were 46 cases among 3300 autopsies. The changes may be classified as cirrhosis, cicatrices, and gummata. Naturally there are various combinations of these. Of these 46 cases, in 23 there were changes described as cirrhotic; 19 showed cicatrices, and 21 gummata. In 8 cases there was a combination of gummata and cirrhosis, in 5 gummata and cicatrices, in 1 cicatrices and cirrhosis, and in 1 all three were present. In only 4 was amyloid change found. In 9 cases there were signs of syphilis found in other organs than the liver. In almost all the cases which came to autopsy the diagnosis was not made during life, the prominent features being due to disease elsewhere. In some a diagnosis was not possible, as there were no symptoms from and no signs of hepatic disease. Old scars in the liver cannot be recognized during life except in rare cases. The cause of death was very various, thus 14 died of cardiac and renal disease, 6 of pneumonia, 3 of acute peritonitis, 3 of tuberculosis, 2 of carcinoma, 2 of aneurysm, 2 of cerebral syphilis, and one each of gangrene, eclampsia, meningitis, accident, leukemia, etc.

*Complaint.* The study of the complaint made by the patient is of interest as showing the diversity of the symptoms for which relief was sought. Many of the patients had lesions other than in the liver. The most common was swelling of the abdomen, in 27 cases. Next in frequency was abdominal pain, usually referred to the upper abdomen, in 18 cases. Jaundice was the complaint in 7, shortness of breath in 5, loss of weight and strength in 3, vomiting in 2, fever in 2, and chills and fever in 3. In certain cases complaint was made of several of these conditions.

*Previous History.* The features which stand out prominently among the general symptoms are as follows: *Loss of weight* was the most frequent and had been more or less marked in 33 cases. The loss varied from fifteen to fifty pounds. Shortness of breath was marked in 10 cases and loss of strength in 9. Seven of the patients had suffered from fever, in 4 associated with chills. Two of the patients with chills and fever had been thought to have malarial fever, and had taken large doses of quinine over long periods. In one case there had been chills and fever over a period of eighteen months. In several of the others a diagnosis of tuberculosis had been made, apparently based largely on the occurrence of fever without any obvious explaining cause. Three patients suffered from severe sweating not associated with chills or fever. Swelling of the legs was marked in 8, but in all was associated with ascites.

Features suggesting disturbance in the abdomen were common. Of these the most frequent was swelling, which occurred in 34 cases, and next abdominal pain in 28 cases. Indefinite gastric disturbance was a feature in 14 cases and vomiting in 14 cases; in 7 of these there had been hematemesis and in 2 melenas. In several of the cases the hemorrhage from the stomach had been very severe. Diarrhea was marked in 3 cases. Jaundice occurred in 17 cases, in some being so intense that there was a greenish tint to the skin.

The duration of the symptoms when the patient came under observation varied from one month to eleven years. The duration was three months or less in 13 cases, three to six months in 11 cases, between six months and one year in 2, from one year to a year and a half in 14, about two years in 7, three years in 4, and eleven years in one. In the others the history was uncertain. In the longer periods the severity of the symptoms was not constant; there were times of improvement and remission.

*Previous Ascites.* This is of particular interest in regard to the general question of cirrhosis of the liver and its prognosis. Seven of the patients had previous attacks of ascites which had required tapping and after which there had been marked improvement so that they gave up treatment. In 3 patients, 2 of whom had been tapped four times, the intervening period was under a year. In 3 patients the interval had been about a year, the number of tapings being one, two, and seven. The remaining patient had been tapped eleven times eleven years before and 86½ liters of fluid removed, and sixteen times ten years before and 134 liters removed. In the intervals the condition had been fairly good. A striking feature in some of these cases was the good general condition despite ascites at intervals over a long period.

*Pain.* This was a marked feature in 34 cases. In 10 it was described as abdominal, in 12 referred to the epigastrium, and in 7 to the upper right quadrant of the abdomen. In 2 it was described as in the right back, in 2 it was said to be in the liver itself, and in one referred to the region of the navel. Several of the patients complained of the pain being worse on lying down.

*Bowels.* No special features were shown. A few of the patients complained of diarrhea and a number described clay colored stools.

*Examination.* The general findings are discussed first and then the special changes in the liver.

*General Condition.* A striking feature was *emaciation*, which was marked in 29 cases, and in some was extreme. A number of other patients had lost some weight but could not be described as emaciated. The appearance of many of the patients suggested severe illness. Jaundice was present in 23 cases. The degree varied from a slight to a marked jaundice, the color of three being greenish yellow. A striking feature was the rapidity of clearing of the jaundice under treatment.



*Fever.* There was some elevation of temperature in all but 7 cases of the series. This is a point of some importance in reference to diagnosis, as the persistence of fever had led to tuberculosis being suspected in some cases. The temperature in about two-thirds of the cases showed constant elevation. In the majority this was not very high, the record being  $99^{\circ}$  and  $100^{\circ}$  and  $101^{\circ}$  F. In some cases it was steadily between  $100^{\circ}$  and  $102^{\circ}$  F. In the other cases the temperature was not constantly elevated but rose each day. In the majority the highest point was not over  $102^{\circ}$  F., but in 3 cases it rose to  $103^{\circ}$  and  $104^{\circ}$  F. In some cases these elevations were accompanied by chills.

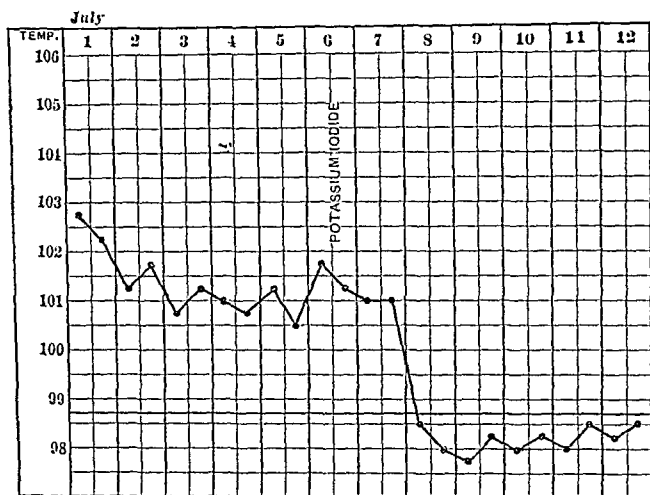


FIG. 1.—Showing the effect of potassium iodide on the fever.

The influence of treatment on the fever was very marked in almost all the cases in which fever was present. In one patient the temperature fell to normal in twenty-four hours and remained there, but the most common period required was forty-eight hours. This was the case in 11 cases. In 5 cases three days were required, and in 5 other cases the temperature reached normal in 6 days or less. This result followed the administration of potassium iodide in the majority of cases; in some mercury was given also, but the most striking results were obtained with potassium iodide alone (Fig. 1).

*Blood.* The average count in 30 cases was: Hemoglobin, 71 per cent.; red cells, 4,380,000 per c.mm., and leukocytes, 8400 per c.mm. In 12 cases the leukocytes were over 10,000 per c.mm., the highest count being 13,000 per c.mm. In only 2 cases was the red count below 3,000,000, the lowest being 2,700,000 per c.mm. In 4 cases the count was between 3,000,000 and 4,000,000. The differential count showed some variation in certain cases, but there were no striking constant peculiarities.

*Ascites.* In 23 cases this was present and usually the fluid was large in amount. Tapping was done in 11 cases. This may seem a small proportion, but one of the striking features is the rapid disappearance of the ascitic fluid under proper treatment without tapping being required. Of the 11 patients one tapping was sufficient in 4, 4 were tapped twice, 1 required to be tapped three times, and 1 was tapped thirteen times. The amount removed at one tapping varied from 2.5 to 22 liters. This last figure seems very large; the patient was admitted twice within six months and was tapped once on each admission, the amounts removed being 19 and 22 liters. She presented a remarkable appearance before each tapping and after it the improvement was striking. She was a colored woman, who refused to remain in the hospital long enough to receive thorough treatment. The specific gravity of the ascitic fluid varied from 1008 to 1020 and the albumin content from 8 to 40 grams per liter. The predominant cells were small lymphocytes. In the only case in which the ascitic fluid was tested for the Wassermann reaction this was not given. Instances of a positive result have been reported.

*Spleen.* This was palpable in 24 cases, in the majority of which the enlargement was marked, in some the edge being several inches below the costal margin. In 8 other cases the area of dulness was increased. The spleen was always hard and firm; in no instance was any irregularity felt; in one case a splenic gumma was found at autopsy.

*Liver.* The changes in this organ are most important in the discussion of the subject. It is convenient to divide the cases into the congenital and acquired.

1. *Late Congenital Syphilis.* Of the late congenital cases there are three instances, which show considerable similarity in the findings. As Rolleston insists we must be very careful not to mistake acquired cases for congenital ones. If acquired it must be at an early age and usually from accidental infection. In these three cases the age of onset of symptoms was two, twelve, and sixteen years. In the first case the mother had two miscarriages, but the child showed no sign of syphilis other than the hepatic condition. In the second there was chronic ear disease dating from the age of four and rhagades at the corners of the mouth. Three other children of the family died soon after birth. In the third case there were no other signs of syphilis, but the father had a syphilitic infection for which he had taken very little treatment.

In these cases the liver showed much the same condition. It was much enlarged generally and showed remarkable, large, rounded, smooth swellings in the epigastrium, which caused distinct prominences (Fig. 2). In one of the patients exploration was done and the mass was found to be a prominence on the surface of the liver which did not differ in appearance from the rest of the organ. It

was distinctly softer than the liver tissue elsewhere and there were many adhesions between it and the abdominal wall. A portion removed for examination showed some increase in connective tissue, but not much more. A positive Wassermann reaction was given by this patient and marked improvement for a time followed the giving of mercury and potassium iodide. He died about four years later, and apparently from the resulting cirrhosis. In 2 of these patients there was in addition a small nodular mass felt on the right lobe. The spleen was much enlarged in 2 and the area of dulness increased in the other. All 3 patients had fever. Ascites was present in 2 of them.

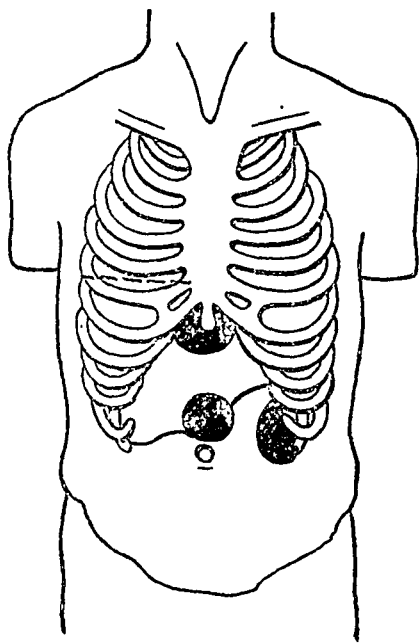


FIG. 2.—Large rounded prominences in late congenital syphilis. Enlargement of spleen

2. *Acquired Cases.* In the study of the tumor one point is worthy of special emphasis, and that is the relatively marked involvement of the left lobe as compared with the right in many of the cases. In 53 cases (3 others being regarded as congenital) the liver was enlarged or showed a tumor mass in 49, and in 23 of these the involvement of the left lobe was strikingly marked in comparison with the right. This is an important point in diagnosis. In regard to the changes in the liver the cases may be divided into three groups.

(a) With general enlargement but no marked gross irregularity of the surface (20 cases). In some cases the liver was slightly irregular.

(b) With definite nodules (20 cases).

(c) Showing a marked prominence which might be described as a boss sometimes associated with nodules elsewhere, but the large smooth enlargement being the striking feature (9 cases). In 3 cases regarded as late congenital this condition was present.

(a) *General Enlargement.* The extent of this varied from an edge which was two inches below the costal margin to cases in which the edge was below the navel. The surface was smooth and the liver hard in the majority; in 2 cases the surface was slightly irregular (Fig. 3). In 8 cases there was complaint of pain and tenderness on palpation. The spleen was enlarged in 12 cases and in 8 ascites was present. There was marked distention of the surface veins in 7 cases. Fever occurred in 14 cases. It is easy to

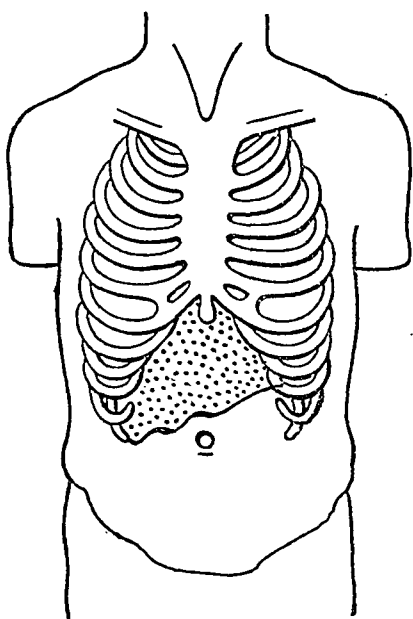


FIG. 3.—General enlargement of the liver, the surface having a slightly irregular character.

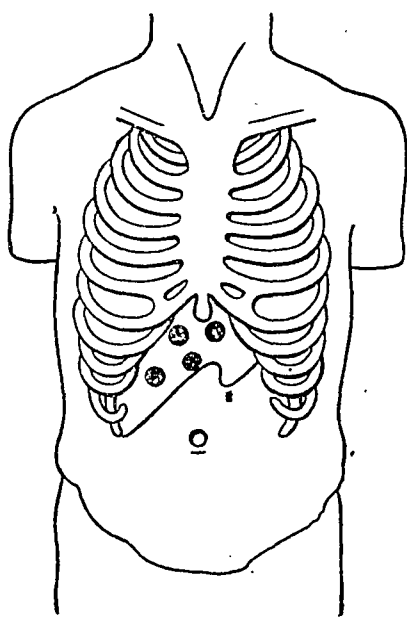


FIG. 4.—Nodules on the surface of the liver.

see that ordinary cirrhosis would be suggested in the cases of this group. Actually, this mistake did not occur in the cases of this group. The incorrect diagnoses were: One was thought for a time to be hepatic abscess on account of fever, chills, and sweats, but the condition was recognized later; 2 had cerebral lues which dominated the picture; 2 had severe cardiac disease, to which the enlargement of the liver was ascribed.

(b) *Nodules.* In the majority these were particularly evident in the epigastrium or in the adjoining part of the right hypochondrium (13 cases) (Fig. 4). In 3 they were more or less general over the surface of the liver and in 3 there was a very large irregular nodular mass. Ascites was present in 10 cases. The spleen was

enlarged in 14 cases. Prominence of the surface veins was marked in 8 cases. Fever occurred in 17 cases. The relatively marked involvement of the left lobe was marked in many of the cases of this group. The error in diagnosis most to be expected would be neoplasm. This occurred in one case, exploration being done, which gave the diagnosis. In one case there was colloid carcinoma of the peritoneum; one was diagnosed as hypertrophic cirrhosis until on a subsequent admission he returned with a tubercular syphilide eruption; one had tuberculosis and the liver condition was regarded as amyloid (which was the case); and in one there was acute leukemia, the diagnosis of syphilis not being made until autopsy. Tuberculous peritonitis was the diagnosis in one case with ascites, the nodules in the epigastrium being regarded as a nodular thickened omentum.

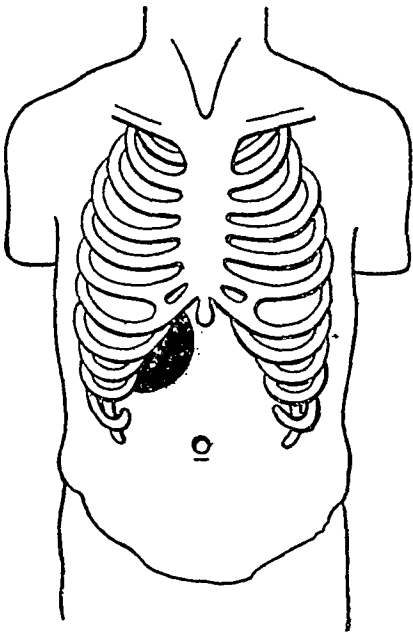


FIG. 5.—Large rounded mass projecting below the right costal margin.

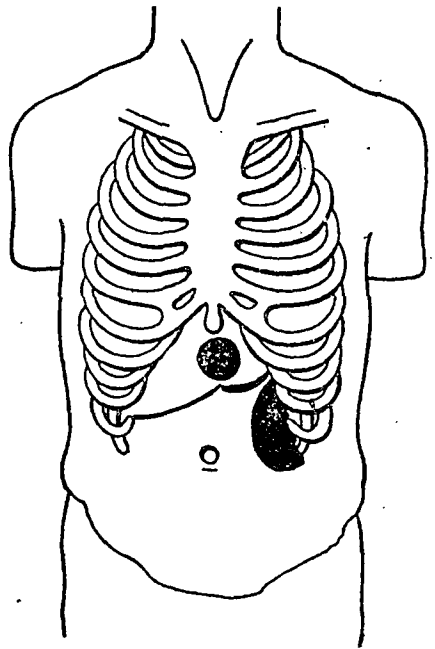


FIG. 6.—Large tumor with a rounded prominence. Marked enlargement of the spleen.

(c) *Rounded Tumor.* The size was enormous in some cases (Figs. 5 and 6), there being a large rounded projection which in some filled the whole upper abdomen. In several instances the enlargement of the spleen was remarkable; in 2 cases the organs practically touched and filled the whole of the upper abdomen. Ascites was present in 4 and the spleen was enlarged in 4 cases. In 1 a friction rub was heard over the mass. Fever was present in 7 cases. Only one error in diagnosis was made, the enlargement being regarded as due to malignant disease. Survival for two years and the appearance of a luetic skin eruption (rupia) gave the correct diagnosis.

*Diagnosis.* This may give difficulty in three principal ways. In the first there is another condition, such as cardiac disease, which seems sufficient to account for the symptoms; this is especially likely to occur if the liver is not specially enlarged or if with enlargement the surface is smooth. In other cases ascites may prevent the recognition of hepatic enlargement. In the second group, disease of the liver is recognized, but its nature is not realized. In the third group some other abdominal condition, such as tuberculous peritonitis, is thought to be present.

1. In 8 cases some other condition was diagnosed. In 3 cases there was cerebral syphilis, the symptoms of which were prominent. In 2 cases tuberculosis, and in the same number cardiac disease was present; in one acute leukemia. In all these the diagnosis was correct so far as it went. In one case the patient had tuberculosis, had been a heavy drinker, and alcoholic cirrhosis was suspected. In 2 cases there was advanced cardiac disease, and in the remaining one leukemia was thought to be the cause of the hepatic enlargement.

2. There were 6 cases in this group. In 2 carcinoma and in 2 alcoholic cirrhosis were diagnosed, and in one each, abscess and gallstones.

3. There were 4 cases, in 3 of which ascites was recognized, but its cause was not determined. In 1 carcinoma of the peritoneum and in 1 tuberculous peritonitis was suspected. One of the other cases was in some ways the most remarkable of the series. The patient was a colored man, aged forty-seven years, who complained of swelling of the abdomen and legs, which began one month before. There had been severe abdominal pain. There were ascites and edema of the legs, but the liver and spleen could not be felt. He died in three days after admission. At autopsy the liver was very irregular and showed a large mass of connective tissue which involved the hepatic vein and inferior vena cava. Many gummata were scattered through the liver.

It may be said that in several cases of 2 and 3, the correct diagnosis was made on subsequent examinations; in all of 3 it was made at autopsy.

*General Symptoms.* As is evident from the study of the symptoms there may be a marked change in the general condition. The patient may have lost weight and strength, be somewhat anemic, have had hematemesis and suffered from abdominal pain. Naturally the possibility of malignant disease comes particularly to mind. The occurrence of fever may suggest some infection. In the cases without any enlargement or evident change in the liver (only 4 in this series) only the knowledge of the possibility of syphilis of the liver, the search for proof of infection (especially the Wassermann test) and the results of specific treatment could give the diagnosis. In this connection the necessity of keeping syphilis in mind as the

cause of more or less continued fever should be emphasized. It is very evident that with advanced cardiac or renal disease, tuberculosis, etc., in the absence of any special hepatic features the diagnosis is not likely to be made.

*Recognition of the Liver Condition.* Here there are several conditions which have to be considered, especially the diagnosis (a) from ordinary hepatic cirrhosis, which is most likely to occur in the cases of uniform enlargement; (b) from newgrowth, either of the liver, or in some cases, in which there is a single nodule, from newgrowth of the stomach. This is most likely in cases with marked nodular changes in the liver. (c) In the cases with the large, smooth, dome-like tumor, abscess or cyst may be considered. (d) Ascites may give difficulty, and it is very important to palpate the abdomen immediately after tapping. It may only be possible then to feel an enlarged liver or a small nodule. Of less importance are (e) amyloid disease, (f) cholelithiasis, (g) splenic anemia, and (h) Hodgkin's disease.

There are some points which deserve emphasis in this connection. One is a history of previous tapping followed by improvement for a time. There were 7 such cases in this series. Another is the finding of relatively marked involvement of the left lobe as compared with the right. This, with any striking irregularity in the organ, should always suggest the possibility of syphilis. The features of the tumor are especially discussed.

(a) *Group with General Enlargement.* This is difficult to distinguish from ordinary cirrhosis, especially as many of the patients give an alcoholic history. Careful examination should be made for any nodular enlargement, and this is particularly important immediately after tapping if there is ascites. In several cases a small nodular mass was felt coming from below the costal margin on deep inspiration, sometimes high up in the costal angle. The liver itself often feels very hard and the surface may be uneven and somewhat rough. Tenderness is sometimes quite marked. It is evident that the distinction from an ordinary cirrhosis is not easy. The knowledge of the possibility of syphilis is perhaps the greatest aid, as it suggests the Wassermann reaction and the therapeutic test. The value of this last is great and of course there need never be any hesitation in doing it, as no harm will result if the condition is not syphilitic. The following is an example of this group:

The patient was a woman, aged thirty-five years, who complained of fever. She had had pelvic infection with a double salpingitis, for which both tubes had been removed some time before. She gave a history of one miscarriage. There had been fever for some months which varied from 99° to 101° F. She had lost considerable weight and at one time the diagnosis of tuberculosis had been made and then again of pelvic infection. At one time on account

of the fever it had been thought that she might have typhoid fever, and the Widal reaction had been done on two occasions, both negative. On examination the patient was emaciated and looked badly. There was no jaundice. The liver was found to be distinctly enlarged and the edge could be felt two inches below the costal margin in the right nipple line. Dulness above in the right nipple line began at the fourth rib. The liver was tender; no nodules were felt. The spleen was markedly enlarged; the edge was felt below the costal margin and was quite hard. There was no rash or evidence of any bone lesions. Diagnoses of typhoid fever, malarial fever, tuberculosis, and septic infection had all been considered. In view of the continued fever and enlargement of the liver it seemed important to consider syphilis. The Wassermann reaction was found to be positive. The patient was put on inunctions and given potassium iodide, and on the third day the temperature dropped to normal and remained there. Within two weeks she had gained 8 pounds and the liver was definitely smaller in size and the edge could just be felt below the costal margin on deep inspiration. The spleen was reduced in size and the edge could just be felt on full inspiration. The patient was seen nine months later; she had gained 25 pounds in weight and looked the picture of health. Neither the liver nor the spleen could be felt.

(b) *The Group with Nodular Masses.* The diagnosis here may be very difficult and a nodule in the liver, particularly in the left lobe, may suggest malignant disease in the stomach or bowel or in the liver itself. As an example of the former the following is quoted:

The patient was a white male, aged thirty-one years. He came complaining of digestive trouble. He had a primary lesion eight years before, but had taken very thorough treatment for five years. His present illness dated back one year. He began to feel badly, complained of pain in the epigastrium and a certain amount of nausea, but no vomiting. He had not been jaundiced. He had lost 25 pounds in weight and on examination was emaciated. There was slight fulness in the left epigastrium and on palpation a small nodular mass could be felt which was quite tender. The edge of the liver was just felt in the right nipple line but could not be positively felt in the median line. The spleen was not felt. After inflation of the stomach the nodule was more easily felt, but its situation was not changed. The note over it was tympanitic. Test meals showed a low total acidity with a mere trace of free hydrochloric acid. The blood count showed a secondary anemia.

The diagnosis was between newgrowth of the stomach and syphilitic nodule of the liver. It was very difficult to tell whether the mass was in the stomach or liver. It was decided to watch the effect of specific treatment, and the patient was given inunctions of mercurial ointment and potassium iodide by mouth. The improvement was very striking; the nodule rapidly disappeared in



size and could not be felt within a month. The patient gained weight rapidly and was soon in perfect health.

The masses on the liver may be regarded as evidence of malignant disease, a mistake which it is easy to make if the general features are marked. The following is such a case:

The patient was a white male, aged fifty-four years, who complained of swelling in the abdomen. His present illness had lasted for about a year and began with nausea and discomfort after eating. Jaundice appeared a few months later. He had lost a great deal of weight and there had been marked abdominal swelling. The patient was emaciated and anemic. The abdomen was much distended with a distinct prominence in the upper part on the surface of which irregularities could be seen. On palpation a hard, irregular, nodular mass was felt, with the lower edge considerably below the navel. A little to the left of the navel a definite notch was felt. The diagnosis of carcinoma was made. The patient did not live in Baltimore, and after discharge he was lost sight of for two years, when it was learned from his physician that the patient was still living and had a well marked skin eruption, regarded as syphilitic.

In one case of this kind an exploration was done to determine the cause of abdominal symptoms, the patient having severe pain. Two gummata were found in the liver.

(c) A variety of other diagnoses may be made. Abscess of the liver may be suspected, particularly in the cases with chills, sweats, and irregular fever. Such a case is the following:

The patient was a white male, aged thirty-eight years, who came with a history of abdominal pain, great weakness, loss of 20 pounds in weight, and fever with sweating for the last six weeks. He had had a good deal of diarrhea. The patient looked very badly, was anemic, and very sallow. He had several attacks of severe pain in the region of the liver, which was somewhat enlarged and quite tender. There was marked tenderness in the seventh interspace, a little outside the right nipple line. The temperature was very irregular, varying from 98° to 102.5° F., and the patient had a number of profuse sweats. Liver abscess was suspected and a number of exploratory punctures were made over the right lobe of the liver, but nothing but blood was obtained. After this the patient was put on potassium iodide with which the improvement was rapid, the pain disappeared and he gained weight and was discharged well.

The *mistakes* in diagnosis which were actually made as regards the tumor are of interest. In other cases, as when cerebral syphilis was present, the diagnosis was correct, but the liver condition was not regarded as important or there was no enlargement of the liver. In 10 cases a wrong diagnosis of the liver enlargement was made. In 2 of these this was carcinoma; in 1 the diagnosis was

corrected by the duration, the appearance of a specific skin eruption, and the result of treatment; in the other case the patient had both carcinoma of the peritoneum and syphilis of the liver, as was found at autopsy. In 2 cases a diagnosis of hypertrophic cirrhosis was made; in 1 the patient returned a year and a half later with a tubercular syphilide, following which the result of treatment was marked. In the second case syphilis of the liver was suspected, but excluded as the Wassermann reaction was negative. Some months later, however, the Wassermann reaction was positive and the diagnosis was also supported by the result of treatment. One case was diagnosed as cholelithiasis and the proper diagnosis reached through the result of treatment over a year later. In 1 case operation was done to determine the cause of persistent pain and enlargement in the upper abdomen, no positive diagnosis having been made. In one case abscess of the liver was suspected, but the result of specific treatment gave the correct diagnosis. Tuberculous peritonitis was the diagnosis in one, the nodules in the left lobe being regarded as the thickened omentum. Enlargement of the liver from cardiac disease was regarded as the cause in one case; this was present and hepatic syphilis as well. In the last of this group practically every possible diagnosis was made by different men. This was regarded as an instance of late congenital involvement, and in many particulars was like a remarkable case reported by Cheney.<sup>4</sup> Hanot's cirrhosis, angioma, adenoma, Hodgkin's disease, and cyst were all considered in addition to cirrhosis. Even after the abdomen was opened it was not possible to be sure of the diagnosis. A positive Wassermann reaction and the response to specific treatment gave the correct diagnosis.

*Therapeutic Test.* There must always be some risk of error in trusting to the result of therapy to make a diagnosis, but in this condition the results are so striking that it has to be included as a method of diagnosis. We have both the general effect, shown particularly on the fever, and the local changes in the liver. As already noted, the effect on the fever is usually very striking, in many cases the temperature falling to normal within forty-eight hours. The influence on the liver itself is almost equally marked; two or three weeks may show a marked decrease in the size of the liver as a whole or of prominences on its surface. In some cases the spleen also shows a remarkably rapid decrease in size. While sometimes the enlarged liver in cirrhosis may show a rapid decrease in size, yet this is not likely to cause confusion.

A knowledge of the condition must be regarded as the most important aid to diagnosis. Other signs of syphilis may suggest the diagnosis. The presence of unexplained fever with hepatic symptoms should suggest syphilis and doing the Wassermann reaction. If in doubt the therapeutic test should always be tried.

<sup>4</sup> Jour. Amer. Med. Assoc., March 26, 1910, liv, 1053 to 1056.

*Course.* Judging from autopsy experience, recovery must be comparatively common. So far as we can decide the hepatic functions are completely restored, as in many patients dying of other diseases and having extensive changes in the liver from syphilis there is no evidence of any disturbance. It is just as certain that a certain number die of the disease and the majority unrecognized. In cases with extensive cirrhotic changes the outlook is practically the same as in ordinary cirrhosis. In such cases we must not expect to do much by treatment.

There were 14 deaths among this series of 56 cases. Of these in only 1 could death be attributed directly to hepatic syphilis. In this case the process caused obliteration of the hepatic veins and inferior vena cava with resulting thrombosis. In 5 cases death resulted indirectly, in 4 from the resulting cirrhosis, and in 1 from amyloid disease. Some of the patients with cirrhosis had received active treatment with resulting temporary improvement. In 1 case death resulted from carcinoma of the peritoneum, in 3 from chronic nephritis and uremia, in 1 from pulmonary tuberculosis, in 2 cerebral syphilis, and in 1 from acute leukemia. In the other cases improvement was the rule as regards the liver condition. Several of these had other serious diseases, such as renal, cardiac, or pulmonary, which affected the general health.

*Treatment.* This is the usual therapy for syphilis with special emphasis placed on the administration of iodide of potassium. In many of the cases this alone was given with a perfect result. No difference could be observed when mercury was added, but it seems wise to give both drugs. Dramatic results, such as almost immediate disappearance of the fever, reduction in the size of the liver nodules, and rapid gain in the general state and weight were seen when iodide alone was given. One patient gained 25 pounds in a month. Salvarsan was given to 3 patients in doses of 0.5 or 0.6 gram, and in 2 of these mercury and iodide were not given in order that the effect could be watched. Improvement followed in both cases, but not as rapidly as was the case with iodide alone or mercury and iodide. In the third case all three were given.

We must recognize that in some cases while we can influence the syphilitic process in the liver we cannot prevent or materially affect the resulting cirrhosis unless the cases are seen early and recognized.

**CONCLUSIONS.** 1. Syphilis of the liver presents a very varied clinical picture with prominent general symptoms in many cases, of which loss in weight is marked. The duration of the symptoms may be prolonged and there may be periods of improvement. Fever is a common occurrence.

2. There are features suggestive of hepatic disease in the majority of the cases. Enlargement or tumor is the most common. This may suggest other conditions, especially malignant disease.

General enlargement and the occurrence of nodules or large rounded masses are the most common. A striking feature is the relatively marked enlargement of the left lobe as compared with the right.

3. The diagnosis may be obscured by other diseased conditions or the liver condition may be interpreted wrongly. Ascites is sometimes a difficulty. Knowledge of the features of hepatic syphilis and the therapeutic test are important aids.

4. Treatment can influence the syphilitic process, but not its results (cirrhosis, amyloid).

---

### MALTOSE IN INFANT FEEDING.<sup>1</sup>

BY JOHN LOVETT MORSE, A.M., M.D.,

ASSOCIATE PROFESSOR OF PEDIATRICS, HARVARD MEDICAL SCHOOL; ASSOCIATE VISITING  
PHYSICIAN AT THE CHILDREN'S HOSPITAL AND AT THE INFANTS'  
HOSPITAL, BOSTON.

THREE different sugars are used commonly in the feeding of infants, lactose, saccharose, and maltose. Maltose is seldom, if ever, used in the pure form. Almost all of the sugars which are spoken of as malt sugars are in reality combinations of maltose and dextrin, for example: Soxhlet's Nährzucker equals maltose 52.44 per cent., dextrin 41.26 per cent.; Löflund's Nährzucker equals maltose 40 per cent., dextrin 60 per cent.; Mead's Dextri-Maltose equals maltose 51 per cent., dextrin 47 per cent.; Maltose of Walker-Gordon Laboratory, equals maltose 57.1 per cent., dextrin 30.9 per cent.; Mellin's Food equals maltose 60.8 per cent., dextrin 19.2 per cent.

These sugars are all disaccharides, lactose being a combination of dextrose and galactose, saccharose of dextrose and levulose, and maltose of dextrose and dextrose. The dextrins are bodies which are formed in the change from starch to maltose. There are a great variety of them and their exact composition is not well known. The dextrins being finally converted to maltose, their ultimate end is dextrose.

The disaccharides are not absorbed as such from the intestine under normal conditions, but are first broken down into their respective monosaccharides by special ferments. These ferments are maltase, saccharase (invertin), and lactase. They are formed in the mucous membrane of the small intestine. Lactase is more abundant in the upper than in the lower portion of the small intestine. Maltase is also present in the blood, the saliva, and the pancreatic juice. Saccharase is present in the intestinal mucous

<sup>1</sup> Read before the American Pediatric Society, May 30, 1912.

membrane at the beginning of the fourth month of fetal life and maltase at the end of the fourth month. Lactase appears in the seventh or eighth month. Lactase is usually the least abundant at birth, but soon increases when milk is given.

The monosaccharides which are formed are taken up by the portal capillaries and carried by the portal vein to the liver where they are converted into and stored as glycogen, to be later reconverted by the maltase in the blood into dextrose and used as required.

If an excessive amount of a disaccharide is introduced into the intestine, or there is a lesion of the intestinal wall, it will pass into the circulation before it is broken down into the monosaccharides. When the disaccharides reach the circulation in this way or are introduced directly into the circulation, all the lactose and the major part of the saccharose are eliminated unchanged in the urine, there being no ferment in the blood which is capable of breaking down these sugars. The rest of the saccharose is eliminated through the gastric mucosa, the salivary glands, and in the bile. The maltose is, on the other hand, broken down by the maltase in the blood, and unless in great excess, is retained. The limits of assimilation of the disaccharides in infancy are: Lactose, 3.1 to 3.6 grams per kilogram; saccharose, no data, probably about the same as lactose; maltose, 7.7 grams per kilogram.

Maltose is the most quickly absorbed of the three disaccharides, saccharose next, and lactose much less rapidly. On the other hand, however, when equal amounts of these sugars are given, considerably more malt sugar is excreted in the feces than milk sugar (Hartje). In fact, under normal conditions lactose is never found in the feces (Péhu and Porcher) unless the food contains more than 7 per cent. of milk sugar (Hartje).

When the disaccharides are added to a food which contains little or no sugar there is a rapid increase in weight, owing to the lessened elimination of water by the kidneys as the result of the presence in the organism of the products of the assimilation of the sugar absorbed. The gain in weight is more rapid with maltose and saccharose than with lactose, probably because of the more rapid absorption of these sugars.

Finkelstein believes that sugar may cause fever, and in his papers has devoted much attention to the so-called "sugar fevers." Leopold found that 43 per cent. of the babies tested with lactose, 42 per cent. of those with saccharose, and 33 per cent. of those with maltose reacted with fever. This fever was, however, always accompanied by diarrhea, and in none of the cases tested in which the stools remained normal did the sugar cause fever. Schlutz's recent experiments make it appear very improbable, moreover, that, even when there are lesions of the intestine, the rise in temperature is caused directly by the sugar.

The disaccharides are all fermentable. Lactose undergoes lactic acid fermentation more readily than the other sugars. Saccharose undergoes alcoholic fermentation most easily and butyric acid fermentation next most readily, while maltose is especially prone to butyric fermentation and next to alcoholic.

It is generally accepted that under normal conditions, and when not given in excess, lactose and maltose have a slightly laxative and saccharose a slightly constipating action. Leopold has recently found that when lactose, saccharose, maltose, and dextrin-maltose mixtures are given to normal or almost normal infants by mouth in equal amounts, the dextrin-maltose mixtures produce diarrhea less easily than the pure disaccharides and that lactose causes diarrhea more easily than either of the other sugars. Sixty-six per cent. of the babies which were given lactose, 21 per cent. of those given saccharose, 16 per cent. of those which received maltose, and only 5 per cent. of those which took the dextrin-maltose mixtures developed diarrhea. The probable explanation of the greater frequency with which lactose caused diarrhea is its relatively slow absorbability.

It has been claimed that the lactose of cows' milk is not identical with that of human milk. There is, however, no convincing evidence in favor of this claim. No differences having thus far been found in the chemical composition of lactose from different sources, it seems more reasonable, therefore, to consider them identical until they are proved not to be.

The normal fecal flora of the breast-fed infant, according to Kendall, is comprised of the following organisms: *Bacillus bifidus*, *Micrococcus ovalis*, *Bacillus coli*, *Bacterium aërogenes*, and *Bacillus acidophilus*. *Bacterium aërogenes* appears in the upper levels of the tract, the duodenum and jejunum; *Micrococcus ovalis* in the lower jejunum, the ileum, and to the ileocecal valve; *Bacillus coli* and *Bacillus acidophilus* in the region of the ileocecal valve, while the *Bacillus bifidus* appears to dominate the ascending and transverse colon. The composition and maintenance of the normal fecal flora is without question due to the relative excess of carbohydrate, in the form of lactose, in the milk. Microscopically with the Gram stain, when babies are fed on cows' milk, there is a relative increase in Gram-negative bacilli of the colon-aërogenes type and of coccal forms of the *Micrococcus ovalis* type, associated with the diminution of the bifidus type. Three butyric acid-forming organisms have been isolated by Passini from the stools of apparently normal bottle-fed babies. These are all anaërobes, and one of them, *Bacillus perfringens* (*Bacterium Welchii*) is a cause of a not uncommon type of infantile diarrhea. This organism has also been found by Sittler and many other observers.

It is, therefore, of great importance, in order to maintain the normal fecal flora, to have a considerable amount of sugar in the

food of babies fed on mixtures of cows' milk. According to Kendall, lactose favors especially the development of *Bacillus bifidus*, which is normally the predominant organism in the large intestine, while maltose is especially conducive to the growth of the *Bacillus acidophilus*, which, although normally present in small numbers, if present in large numbers is liable to produce an excessive degree of acidity which may cause irritation of the intestine and an intolerance for sugar. Under normal conditions, therefore, as far as regards the maintenance of the normal intestinal flora, lactose is preferable to maltose.

Although maltase is formed before lactase, lactase is present at birth and becomes abundant as soon as milk is given and there is any need of it. The early appearance of maltase is, therefore, no argument in favor of the use of maltose instead of lactose. The presence of maltase in the blood is no argument in favor of maltose as a food. The maltase is in the blood to break down the maltose formed from glycogen, not to break down sugars in the intestine. It is impossible, moreover, for it to get into the intestine. The assimilation limit of lactose is, it is true, lower than that of maltose. This limit is, however, at least three times as large as would ever be given in a properly modified milk. The higher assimilation limit of maltose is therefore of no practical advantage. In spite of its higher assimilation limit, moreover, more maltose than lactose is excreted in the feces when equal amounts are given by mouth. The more rapid immediate gain in weight when maltose is added to a food poor in sugar than when lactose is added is of no importance, since the gain in both instances is almost entirely due to the retention of water. Even if it is true that the so-called "sugar fever" is really due to sugar, the fact that the rise of temperature occurs more often with lactose than with maltose does not count in favor of the use of maltose rather than lactose in the feeding of normal infants, because fever never occurs unless there is a diarrhea which shows some lesion of the intestine. Neither is the fact that large amounts of lactose cause diarrhea more easily than maltose and the dextrin-maltose preparations of much importance, because such large amounts of lactose should never be given. The less rapid breaking down and the consequently slower absorption of lactose than of maltose is of great importance in maintaining the normal fermentative flora throughout the intestinal tract. Few organisms other than those normal to the intestinal tract of infants can utilize lactose before it is broken down, many can utilize maltose. Lactose is especially suited to the growth of the *Bacillus bifidus*, the organism normally predominant in the large intestine; maltose to the development of the *Bacillus acidophilus*, which, when in excess, may cause disturbance. It is not necessary, therefore, to bring forward the argument that lactose is the only sugar present in human milk and in the milk of other animals and that it must be

therefore the natural sugar for an infant, because, in the light of the evidence just cited, there can be no doubt that lactose is preferable to maltose for the feeding of normal infants.

Finkelstein and Meyer believe that the diarrheal diseases of infancy originate in a functional weakness of the intestine, that this functional weakness is kept up and increased by fermentation, and that sugar is the special and primary cause of fermentation. Neither normal or abnormal acidification can take place without primarily. It is injurious in that it causes an acid fermentation. The fermentation of the sugar is dependent on two main factors: The concentration of the whey, and the relative proportions of casein and sugar in the mixture. They conclude, therefore, that the principles on which the preparation of a food to combat intestinal fermentation depend are: A diminution in the quantity of milk sugar; a diminution of the salts through dilution of the whey; and an increase in the casein, with varying, and, under certain circumstances, not inconsiderable amounts of fat. They subsequently developed a food to meet these indications, to which they gave the name "Eiweissmilch." This food is prepared with precipitated casein and buttermilk, after which it is boiled. Its composition is: Fat, 2.5 per cent.; lactose, 1.5 per cent.; proteid, 3 per cent.; salts, 0.5 per cent.

They claim that with this mixture the loose, green stools are quickly replaced by typical soap stools. One quart of this milk contains, however, only about 370 calories. Babies taking it suffer, therefore, from lack of nourishment. They advocate, therefore, the addition of malt sugar or the dextrin-maltose preparations to the mixture after the disappearance of the acute symptoms in order to avoid loss of weight and disturbance of nutrition. They claim that, on account of its more rapid absorbability, maltose does not cause a recurrence of the symptoms of fermentation.

Finkelstein and Meyer's arguments point strongly to sugar as the etiologic factor in intestinal fermentation. Their treatment of fermentative conditions with a food low in sugar and high in proteids is therefore a rational one. The substitution of dextrin-maltose mixtures for lactose also seems rational. It does not seem rational, however, to treat all cases in the same way or to give all babies the same food without regard to their individual digestive capacities. The lactic acid in the buttermilk also seems irrational in that it is one of the products of the fermentation of lactose and, therefore, presumably one of the substances causing the disturbance in the intestine.

It seems wiser to take advantage of the main principles of this method of treatment of the intestinal fermentative conditions and avoid the disadvantages of a routine food and the unnecessary, even if not harmful, lactic acid. It is possible by using mixtures of precipitated casein, prepared according to Finkelstein and



Meyer's method, water and cream to obtain any desired percentages of fat and casein with extremely low percentages of lactose and salts. Any of the dextrin-maltose preparations can then be added in any quantity desired. The use of this method of treatment in a considerable number of cases during the last year has convinced me that there is a variety of intestinal indigestion in infancy which is relieved by reducing the sugar and salts in the food to a minimum and giving large amounts of casein and that the dextrin-maltose preparations can be given to these patients sooner than lactose without causing a return of the symptoms. This type of intestinal indigestion may be either acute or chronic and is characterized by an increased number of stools of diminished consistency, green in color, often frothy, acid in reaction, and not infrequently containing mucus and fat curds. Unfortunately, however, precisely similar stools may be seen in other conditions in which the trouble is due primarily to bacteria and in which this method of treatment may do material harm. It is to be hoped that with increasing knowledge of the bacteriology of the intestinal tract in infancy some simple methods will be evolved which will make it possible to readily differentiate between the diarrheas due primarily to chemical changes in the intestinal contents and the disturbances of the digestive functions dependent on them and those due primarily to bacteria. At present it is extremely difficult to distinguish between them and correspondingly hard to know how to treat them.

There is a type of diarrhea in infancy, usually characterized by watery, green, foamy, irritating stools, but sometimes with discharges of mucus and blood, which is associated with the presence in the intestinal contents of large numbers of bacilli belonging in the group of which the *Bacillus perfringens* and the gas bacillus (*Bacterium Welchii*) are members. These organisms ferment the common disaccharides and liberate considerable amounts of butyric acid. Large amounts of sugar are, therefore, contraindicated in this group of cases, maltose being more harmful than lactose because it undergoes butyric acid fermentation more readily. This type of diarrhea yields most rapidly to buttermilk and mixtures containing living lactic acid bacteria with a small amount of lactose. The lactic acid forming organisms kill out the pathogenic organisms. Being themselves fermentative organisms, they cannot develop in a protein medium. A moderate amount of lactose must, therefore, be present in the food.

It has been shown by Theobald Smith, Kendall, and others that when bacteria act upon carbohydrate and proteid substances they produce from the former fermentative products and from the latter putrefactive substances. The fermentative process takes precedence over the putrefactive if both carbohydrate and proteid are present together in the medium in which they are. The products

of the fermentation of carbohydrates are practically harmless, while the products of the decomposition of proteids are actively toxic. In the diarrheal diseases due to organisms, such as the dysentery bacillus, which produce toxic substances from protein, it is therefore of great importance to have an excess of readily fermentable carbohydrate in the food to change the character of the bacterial activity from the proteolytic to the fermentative type. This is most easily accomplished by the feeding of the disaccharides, which are preferable to the monosaccharides, because they are more readily procured and especially because they are less rapidly absorbed from the intestinal tract, and to the polysaccharide, starch, which, if given in sufficient amount to accomplish the desired result, is almost certain to disturb the digestion. Starch is broken down so slowly, moreover, that there is never a sufficiently great concentration of sugar at any time. Lactose is preferable to maltose for several reasons. It is, in the first place, more slowly broken down and absorbed and consequently exerts a more prolonged action. In the next place, few organisms, except those normal to the intestinal tract of infants, can utilize it before it is broken down by hydrolysis. There is also danger, as already pointed out, if maltose is given freely, of encouraging the overdevelopment of the *Bacillus acidophilus* and developing a sugar intolerance.

**CONCLUSIONS.** Lactose is for many reasons preferable to maltose for the feeding of normal infants. There is a type of intestinal indigestion due to the fermentation of sugar in the treatment of the convalescent stage of which maltose is better borne than lactose. Maltose is contraindicated in the treatment of diarrheas due to the gas bacillus and similar organisms, and is less useful than lactose in the treatment of those caused by the dysentery bacillus.

#### BIBLIOGRAPHY

- Borrino. *Riv. di Clin. Ped.*, August, 1910.  
 Finkelstein and Meyer. *Jahrb. f. Kinderheilk.*, 1910, lxxi, 525 and 683; *Berlin. klin. Woch.*, 1910, lvii, 1165; *Münch. med. Woch.*, 1911, lviii, 340.  
 Hammersten. *Text-book of Physiological Chemistry*, New York, 1911.  
 Hartje. *Jahrb. f. Kinderheilk.*, 1911, lxx, 557.  
 Ibrahim. *Hoppe-Seyler's Zeitsch. f. phys. Chemie*, 1910, lxvi, Nos. 1 and 2.  
 Kendall. *Jour. Med. Research*, 1911, N. S., xx, 117; *Boston Med. and Surg. Jour.*, 1911, clxiv, 288.  
 Kendall and Smith. *Boston Med. and Surg. Jour.*, 1911, clxiv, 306.  
 Leopold. *Zeitsch. f. Kinderheilk.*, 1910, i, 217.  
 Morse. *Amer. Jour. Dis. Children*, 1911, ii, 315.  
 Morse and Talbot. *Boston Med. and Surg. Jour.*, 1911, clxiv, 852.  
 Nothmann. *Zeitsch. f. Kinderheilk.*, 1911, ii, 563.  
 Péhu and Porcher. *Arch. de Méd. des Enfants*, 1911, xiv, 113.  
 Schlutz. *Amer. Jour. Dis. Children*, 1912, iii, 95.

## BISMUTH POISONING.

BY LOUIS M. WARFIELD, M.D.,

MILWAUKEE, WISCONSIN.

It seems rather strange that there should be no adequate discussion or description of the lesions caused by intoxication with bismuth in any modern text-book on medicine. Even in Edsall's exhaustive article on metallic poisons in Osler's *System of Medicine* there is no mention of the effects of bismuth upon the human system. This is all the more remarkable in view of the fact that evidences of systemic poisoning by bismuth are scattered through the literature of the last few years, especially since the advent of the  $x$ -rays in the diagnosis of gastro-intestinal diseases and of bismuth paste (Beck's) in the treatment of chronic suppurating, non-bacterial sinuses.

A case of bismuth poisoning following the injection of about 2 ounces of bismuth subnitrate paste into an iliopsoas abscess, revealed the utter absence of data on the subject in an available form, and constitutes the excuse for the present *resume* of the subject.

EXPERIMENTAL DATA. As long ago as 1786 there were reports of vomiting, diarrhea, twitchings, dizziness, and somnolence due to the ingestion of bismuth salts. It was thought that these symptoms were due to impurities, particularly arsenic and lead, in the preparations of bismuth used, and it is possible that such was the case at that time.

Even before Kocher, in 1881, recommended bismuth subnitrate salve in the treatment of burns and granulating wounds, there had been some experimental evidence that bismuth salts were not altogether harmless.

Feder-Meyer,<sup>1</sup> in 1879, investigated the subject. He says that according to Orfila, all bismuth preparations containing oxygen are toxic, whether taken internally or injected into a vein. Feder-Meyer produced acute and chronic poisoning in rabbits by injecting soluble ammoniated bismuth citrate subcutaneously or by introducing it into the stomach through a tube. In acute poisoning the animals had convulsions and incoördinated movements ending in death. There was fall of blood pressure and of body temperature. In chronic poisoning the animals were restless and lost weight. When the dose was increased, there were twitchings and diarrhea ending in convulsions and death. He found that the subcutaneous injection of from 6 to 9 milligrams of the salt per kilo body weight, caused death of the animal. The heart

<sup>1</sup> Inaug. Dissert, Würzburg, 1879.

muscle and liver showed fatty degeneration. In the mucous membrane of the stomach there was pigmentation due, he thought, to extravasation of red blood cells, and in most of the organs there were demonstrable quantities of bismuth. He thought that death was due to poisoning of the nerve centres.

Mory,<sup>2</sup> in 1883, repeated the experiments of Feder-Meyer using the same bismuth salt, but he regarded the death of his animals as a heart paralysis. In cats and dogs the subcutaneous injection of 0.15 gram ammoniated bismuth citrate caused vomiting and diarrhea. In chronic poisoning he saw increasing destruction of the skeletal muscles and thought that the paralysis was due to this condition. He concluded that the bismuth salts are also intense poisons to the higher animals. In warm-blooded animals we can explain all the symptoms by the action of bismuth upon striped muscle. The longer the poisoning lasts the more intense the gastro-intestinal symptoms become. There is marked hyperemia of the intestines accompanied by a fall in blood pressure. The animal dies because the heart has no resistance against which to work.

Luchsinger<sup>3</sup> experimented upon rabbits, cats, and dogs, and came to the same conclusions as Mory.

In 1886, Dalché<sup>4</sup> reported 2 cases of bismuth poisoning in humans characterized by black line on the gums and white diphtheritic membranes. There was bismuth in the urine. He and Villejean<sup>5</sup> instituted a series of experiments on the toxicity of bismuth subnitrate. Already the nephritis, enteritis, and stomatitis with discoloration of the gums had been attributed by observers to the bismuth salts. Dalché himself, however, in his case reports had suggested that impurities, particularly lead and arsenic, were to be considered as factors. These observers satisfied themselves by careful analysis of the purity of their bismuth salt. They found that they could give to a normal dog 10 grams of the subnitrate daily for a month, in all 300 grams, without noting any ill effects. But when the salt was put on a raw surface of any extent, intoxication often followed. Having shown the toxicity of the salt, they injected dogs subcutaneously with doses of 0.3 gram to 3 grams. For example, one dog on twelve successive days received subcutaneous injections of the salt. It died on the thirteenth day. Five days before death there was noticed on the gums of the anterior molars, on the mucous membrane of the inferior maxilla, at the external alveolar border, a brownish-violet, glistening, serrated line and two brownish-violet spots were seen on the mucous membrane of the left cheek not far from the commissure. The follow-

<sup>2</sup> Inaug. Dissert., Bern, 1883.

<sup>3</sup> Mittheil. d. Naturf. Gesellschaft in Bern, 1882-1883, p. 26.

<sup>4</sup> Annales d'Hygiene Publique et de Méd. Légale, 1886, xvi, 358.

<sup>5</sup> Arch. Gén. de Méd., 1887, xx, 129.

ing day, the eighth, similar spots appeared on the mucosa of the right cheek and the gingival serrated border was advancing. During the succeeding days the serrated border extended upon the anterior gums of the lower jaw and appeared upon the buccal, labial mucosa, and on the inferior surface of the tongue. The oldest lesions became superficially gangrenous and presented softened grayish-white plaques surrounded by a slight areola of a brownish-violet color. At autopsy, besides the lesions described, there were seen enormous superficial gangrenous plaques upon the buccal side of the cheeks. The urine contained no albumin and the kidneys showed nothing but vascular congestion.

A second dog also showed lesions on the gums and on the mucous membrane of the cheeks.

They found that bismuth was eliminated through the salivary glands and that the presence of albuminoid substances favored the solution of the bismuth when in an ordinarily insoluble form such as the subnitrate.

Dalché and Villejean remark that the most striking feature of bismuth poisoning is the stomatitis. It is characterized by a lesion on the gum of a blackish or brownish-violet shiny character, and by spots of similar color on the internal surface of the lips and cheeks. It may remain stationary but in advanced stages the mucosa of the gum margin is softened, the teeth are, at times, loosened and the mucous membrane softens, becomes pulpy and covered with a grayish or whitish-gray membrane surrounded by a blackish areola. These sloughs may separate and ulcers result.

The lesion usually begins at the level of the molars opposite the opening of the parotid gland duct. This is a point common to both bismuth and mercurial stomatitis, as well as the ulcer beneath the tongue where it is in contact with the teeth. In both forms of poisoning salivation is profuse and the breath has a fetid odor.

The stomatitis may follow a few days after the bismuth injection. They conclude that subnitrate of bismuth absorbed from subcutaneous injection or from the surface of a wound, can cause acute intoxication due directly to bismuth. This absorption is due to the presence of albuminous material favoring the solubility of the metallic oxide, although slowly, it produces poisoning because it is continuous. The accidents, stomatitis, nephritis, enteritis, etc., are dependent upon the paths of elimination of the metal.

In a further series of experiments Dalché and Villejean<sup>6</sup> produced chronic poisoning in dogs by injecting 0.25 to 0.50 gram subcutaneously at intervals of a few days for three months. Hemiplegia and stomatitis with a black line on the gums developed and the dog, after becoming weak and emaciated, died. At autopsy the

<sup>6</sup> Bull. de Therapeutique, Paris, 1888, cxv, 404 and 448.

stomach and intestine were full of bile. The large intestine showed pseudomembranous colitis with the usual blackish discoloration; there were congestion and ecchymoses. The liver and kidneys were congested. Careful examination of the peripheral nerves and of the anterior roots revealed nothing abnormal.

They call particular attention to the similarity of stomatitis caused by lead, mercury, and bismuth, lead being less severe because it is not easily absorbed except under certain conditions of peculiar susceptibility. Mercury stands midway between lead and bismuth. The stomatitis may be mild or fatal. All produce dysenteric stools, all act as cholagogues, all produce kidney lesions of greater or lesser severity depending on the dose and on the susceptibility of the animal. They say it is a striking fact that chemically lead, mercury, and bismuth have high atomic weights, 206.4, 200, 210 respectively. They suggest that possibly all the heavy metals copper, platinum, iridium, gold, if absorbed in sufficient quantity would produce similar lesions. Normally bismuth subnitrate is not soluble in the juices of the alimentary canal. Its sojourn in the intestines is short. Two factors concur in rendering bismuth soluble when injected subcutaneously: (1) Profound changes which take place when bismuth oxide comes into contact with tissue juices rich in albumin; (2) the continuous absorption of small amounts now rendered soluble.

Balzer<sup>7</sup> confirmed the work of Dalché and Villejean except that he used citrate of bismuth. He did not think that the stomatitis due to the bismuth is similar to that due to mercury. The bismuth tends more to a membranous formation and appears deposited on the margins of the gums. There is also not so much loosening of the teeth with bismuth and not so much pus due to growth of mouth bacteria. He found that bismuth was eliminated in the urine, bile, and saliva.

Pisenti<sup>8</sup> in an experimental study of the action of bismuth on the organs of the rabbit, found that there were lesions in various organs. In the kidneys there was necrosis of the epithelium of the convoluted tubules. In the digestive system there was partial hyperemia and partial pigmentation without destruction of the mucosa. The liver cells were the seat of fatty degeneration.

Mayser,<sup>9</sup> in a long article, quotes from all the literature up to 1892, and adds some experimental data of his own. He considered that the black pigmentation in the large intestine was due to bismuth sulphide and not to extravasated blood, as Mory and Feder-Meyer had thought. Chemical examination showed bismuth in the blood, urine, stomach, small and large intestine, and kidneys, but not in the bile, brain, or muscles. He concluded from his experi-

<sup>7</sup> Comptes Rendus d. Séances et Mémoires de la Soc. de Biol., Paris, 1889, n. s., 1, 537.

<sup>8</sup> Annali Università Libera di Perugia, 1887-1888, iii, 87 to 106.

<sup>9</sup> Inaug. Dissert., Freiburg in Baden, 1892.

ments that bismuth has a poisonous effect on the kidneys causing necrosis of the tubular epithelium and a production of casts. The necrosis proceeds slowly and does not lead to great loss of substance. He saw calcified deposits here and there. At times one-half of the kidney contained them, the other half was free. The glomeruli were, at times, calcified. He compared his findings to those produced by chromic acid and mercury nephritis. The calcification found was apparently caused by long-standing, mild poisoning. The most severe changes followed subcutaneous injections, due to the better absorption of bismuth when given in this manner.

Although there are some minor differences in the conclusions of these authors, they are in substantial agreement concerning the toxicity of bismuth when given to animals. In all cases great care was taken to employ only absolutely, chemically pure bismuth salts.

Böhme,<sup>10</sup> in 1907, reported a fatal case of poisoning following the internal administration of bismuth subnitrate, in which the symptoms were violently acute and were like those described by Collishon in nitrite poisoning. There was methemoglobinemia before the child died. This led him to investigate the breaking up of bismuth subnitrate in the intestinal canal. Collishon had already stated his belief in 1889 that the toxic symptoms due to nitrite poisoning and those due to poisoning following the administration of bismuth subnitrate were the same. He, therefore, thought that the nitrites, not bismuth, were responsible for the symptoms.

Böhme showed that bismuth subnitrate in contact with the feces liberated nitrites. He also found that when colon bacilli were grown in bouillon to which bismuth subnitrate was added, that nitrites were formed. Since Böhme's report several fatal cases have been published in all of which there were cyanosis, collapse, diarrhea, and the blood was of a chocolate color before death. The color was due to methemoglobin. In certain cases of intestinal disease the administration of bismuth subnitrate followed by death may be due to the sudden liberation of nitrites, but it cannot be doubted that, in view, of the experimental evidence, bismuth is the toxic agent in the chronic forms surely and in the fatal cases where it has been applied to raw surfaces as bismuth paste.

CASE REPORT. L. N., Hosp. No. 10068, a white girl, aged nine years, of Finnish parents, was admitted to the Milwaukee County Hospital, September 9, 1911, complaining of sore mouth. Her home surroundings have always been of a squalid kind. Both parents probably have syphilis, one certainly had syphilis before this child was born. One sister, aged seven years, died in this hospital of generalized tuberculosis. The patient had never been

<sup>10</sup> Arch. f. exper. Path. u. Pharmacol., Leipzig, 1907, lvii, 441 to 452.

a robust child. In January, 1910, she was in a hospital on account of a weak back. A diagnosis of tuberculosis of the spine was made and she lay on a Bradford frame for one year. During 1910, there was an iliopsoas abscess which pointed at the front of the leg opposite the lesser trochanter. This abscess was twice incised, once above Poupart's ligament, once below. In November, 1910, about 2 ounces of bismuth subnitrate paste (Beck's) were injected into the sinus. The opening of the sinus in the leg below the groin promptly closed and no paste ever was extruded. Within two weeks a black line was noticed at the gum margins. This has persisted, becoming occasionally more prominent, again less noticeable. In August, 1911, a "sore" started in the right cheek opposite the upper second molar tooth. Later there was ulceration of the right side of the tongue.

On admission the child was enveloped in a plaster cast from armpits to the crests of the ilia. On examination, after removal of the cast, she was seen to be well nourished and of normal size. There were evidences of old rickets on the head and chest. The chest was, however, fairly well formed, but flaring below. There was slight impairment of the percussion note beneath the left clavicle with prolongation of expiration. There was a scar about 3 cm. long in the right iliac fossa and a small puckered scar on front of the right thigh. The spleen was palpable. There was general glandular enlargement, especially a large collection of glands beneath the ramus of the right mandible causing a visible swelling. The breath was very fetid, the teeth yellowish, many were decayed, especially those of the lower right jaw. The front teeth were not notched but were roughened both laterally and on the edges.

On the gum margins of both jaws both on the inner and outer sides there was a dark violet-black line averaging 1.5 mm. in depth, which did not quite reach the free border of the gum margin (Figs. 1 and 2). This line was smooth and somewhat glistening. The teeth were not loosened and there was very little pyorrhea alveolaris. The tongue was heavily coated with a brownish fur. Along the whole right edge of the tongue extending nearly to the tip was a bluish- or violet-black discoloration which in its widest part was 2 cm. and extended toward the dorsum and ventral surfaces for a short distance and having rather sharply defined margins. Along the very edge of the tongue in the centre of the discoloration was a white, opaque, serrated membrane, which was adherent to the underlying tissues. On the buccal surface of the right cheek were two discolored plaques, one near the angle of the mouth and one (the earlier one) with its centre about opposite the upper second molar tooth. This latter was 2.5 to 3 cm. in diameter, the former was irregular in outline and smaller. They had exactly the same appearances as the ulcer on the tongue.



The blue discoloration was sharply demarcated from the surrounding fairly healthy mucous membrane. White necrotic serrated membranes covered about half of each ulcer, the centre of the patch corresponding to the centre of the necrotic cap.

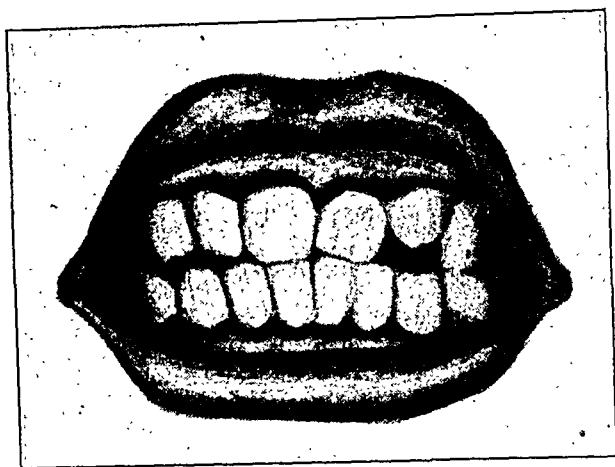


FIG. 1.—Showing the line on both gums and the somewhat notched incisors.

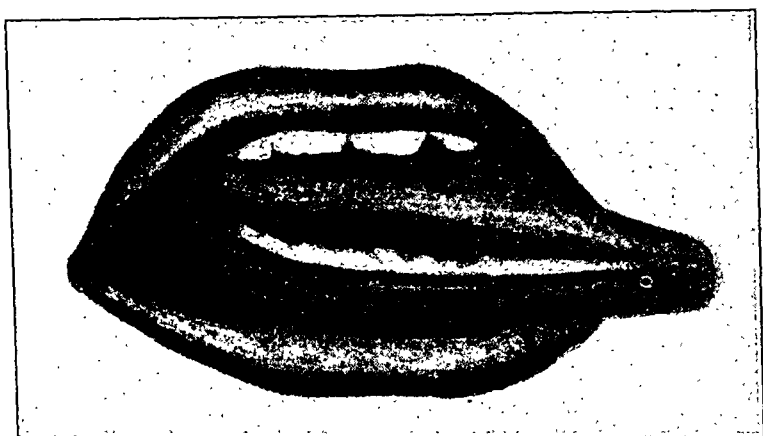


FIG. 2.—Extensive ulceration of the tongue with the diphtheritic membrane.

An *x*-ray of the right lumbar region (Fig. 3) showed an irregular shadow in the lumbar muscles about 10 cm. long and 2 to 4 cm. broad from which delicate shadows ran to the opening of the sinus in the upper leg. This was evidently about 2 ounces of bismuth paste which did not appear much encapsulated.

The Noguchi reaction was negative on two occasions. The red blood corpuscles were, 5,600,000; leukocytes, 14,600; hemoglobin, 90 per cent. (Sahli) on admission. (The leukocytosis was evidently due to the alveolar abscess on the right side.) The differential count of the white cells showed nothing abnormal. The urine was of 1020 to 1025 specific gravity, contained no

albumin nor casts, and on several examinations no bismuth could be found.

The patient gradually improved. The ulcers in the mouth became less foul, the breath became much less fetid. When she left the hospital, February 19, 1912, the following note was made: The condition has practically cleared. The tongue is perfectly clean on the right margin. On the right cheek is a very slight



FIG. 3.—Sketch from x-ray plate showing location of bismuth.

violet discolored area corresponding to the large spot of ulceration. The breath is no longer disagreeable. The line on the gums, both within and without is still present.

This case is almost the exact counterpart of those reported by Gaucher and Ballé.<sup>11</sup> They record the fact that Kocher in 1881, after his recommendation of bismuth for dressing wounds, reported

<sup>11</sup> Bull et mém de Soc des Hôp de Paris, Paris, 1895, s. 3, xii, 773.

4 cases of poisoning, in 1 of which a blackish discoloration appeared on the gums at the alveolar dental border the day after the dressing to a large raw surface. Petersen in 1883, they remark, also observed a case in a girl, aged fourteen years, following operation and dressing with bismuth subnitrate. There was stomatitis and salivation.

Among other case reports are those of Mahne,<sup>12</sup> E. G. Beck,<sup>13</sup> David and Kauffman,<sup>14</sup> Don,<sup>15</sup> etc.

**SYMPTOMS.** From the cases reported we can deduce a rather typical picture which differs from the poisoning of lead and of mercury.

There are three stages: (1) Benign, where the violet-black line is the only manifestation; (2) moderately severe, where there is stomatitis, more or less acute, to which succeeds a chronic stomatitis characterized by discoloration of the gum margins and tattooing of the mucosa which extends to the buccal cavity; (3) a severe form characterized by a longer duration of the stomatitis, the margins of the gums and tattoo-like plaques ulcerate, secondary infections supervene, and general symptoms as fever, hiccough, vomiting, diarrhea, and albuminuria occur.

Prodromal symptoms are slight or, if present, there is only malaise, slight salivation or tenderness about the mouth. There soon follows the line on the gums or tattoo plaques and ulcerations on the buccal mucosa. The bismuth line occupies a part or all of one or both jaws. It resembles the lead line but differs from it because of its really violet tint. In benign cases the gum margin is not swollen. In severe cases there may be swelling, ulceration, and loosening of the teeth. Cessation of the bismuth treatment brings about improvement, but the gums still retain the discoloration for some time.

The line on the gums is usually the first symptom of the poisoning, but occasionally there are plaques on the buccal mucosa like tattoo marks. The bismuth plaques may be found anywhere in the mouth but show preference for sites where the teeth and gums come in contact and the first plaque is often at or near the opening of the duct of the parotid gland. The ulceration is more apt to occur at this situation. The sides of the tongue are also frequent sites of ulceration.

The color is the same in all, a violet black. The lesions rarely appear insidiously, but are usually preceded by salivation and erythematous stomatitis. At times the lesions come on rapidly with edema.

The spots may be simply small areas of bluish violet-black color, in severer cases there is some swelling and a diphtheritic

<sup>12</sup> Berl. klin. Woch., 1905, xlii, 232.

<sup>13</sup> New York Med. Jour., 1909, lxxxix, 16.

<sup>14</sup> Illinois Med. Jour., 1909, xvi, 370; Jour. Amer. Med. Assoc., 1909, lii, 1035, 1953.

<sup>15</sup> British Med. Jour., 1909, i, 1481, and 1908, ii, 1604.

white membrane in the centre. This is characteristic of bismuth. In very severe cases gangrene occurs with resulting loss of substance.

The breath is usually foul, depending upon the state of the lesion.

The spots appear simultaneously or in crops. They cause more or less functional disturbance and thus tend to weaken the patient. Mastication may become impossible. The swollen and painful tongue may with difficulty be protruded. Ulcerations on the soft palate and tonsils may cause hoarseness. Salivation is marked and when healing of ulcers begins the saliva may be so tenacious as to interfere with swallowing. The patient in these severe types naturally emaciates, and there is often fever due to secondary infections. There also may be dysphagia, vomiting, and diarrhea. The urine may even be blackish and frequently contains bismuth. Occasionally albumin and casts are present. These symptoms are produced by a pure bismuth salt. They are not the result of impurities, such as lead, arsenic, or antimony.

THE CAUSE OF THE POISONING. Our views in regard to the toxicity of the bismuth preparations have undergone a marked change since von Bardeleben wrote, in 1892, that of one thing we were sure; that was that even applications of magisterium bismuthi to large raw surfaces would not cause symptoms of poisoning unless the preparation were impure. Since then, and even before then (Kocher), there have been numerous reports of poisoning by bismuth until a fatal case reported in 1906 by Benneke and Hoffman<sup>16</sup> in a child, aged three weeks, to whom bismuth subnitrate had been given for x-ray examination, and a fatal case reported by Böhme,<sup>17</sup> in 1907, led Böhme to investigate the subject carefully. His results have already been outlined.

Since then others, among whom are Novak and Gutig,<sup>18</sup> Meyer,<sup>19</sup> E. G. Beck,<sup>20</sup> and Zabel,<sup>21</sup> have reported cases, some fatal, some showing marked collapse with recovery, in which methemaglobin was shown to be present in the blood in some cases. These authors are firm in their belief that the splitting of the subnitrate into nitrites is responsible for the toxic effects and they call it nitrite poisoning. Beck goes so far as to say that the line on the gums is a good sign. He has injected 720 grams (!) of 33 per cent. paste into the pleural cavity. Symptoms of poisoning set in and he removed the paste. Recovery followed.

Schumm<sup>22</sup> and Lorey<sup>23</sup> have been able to demonstrate frequently methemaglobin by means of the spectroscope in the blood of

<sup>16</sup> Münch. med. Woch., 1906, liii, 945.

<sup>17</sup> Loc. cit.

<sup>18</sup> Berlin. klin. Woch., 1908, xlv, 1764 to 1768.

<sup>19</sup> Therapeutische Monatshefte, 1908, xxii, 388 to 390.

<sup>20</sup> Jour. Amer. Med. Assoc., 1909, lii, 14 to 18; Zentralbl. f. Chir., 1910, xxxvii, 601 to 606.

<sup>21</sup> Deutsch. med. Woch., 1909, xxxv, 200.

<sup>22</sup> Ibid., 1910, xxxvi, 1250.

<sup>23</sup> Ibid.

those taking large doses of bismuth subnitrate, a fact not until then known. None could be found with therapeutic doses of the subnitrate and none could be demonstrated when large doses of bismuth carbonate or oxychlorate were administered. They deny the contention of Lewin that bismuth subnitrate poisoning is due only to the bismuth.

On the contrary, there is considerable experimental work with various bismuth salts in which the symptoms have been practically similar. Thus ammoniate citrate of bismuth (Feder-Meyer,<sup>24</sup> Mory<sup>25</sup>), subnitrate (Dalché and Villejean<sup>26</sup>), bismuth sodium tartrate (Mayser)<sup>27</sup>, bismuth oxide and bismuth carbonate (Steinfeld and Meyer<sup>28</sup>) have been shown to produce acute or chronic poisoning in animals. Dermatol and Airol have produced symptoms of bismuth poisoning (Glaser,<sup>29</sup> Weissmüller,<sup>30</sup> Aemmer,<sup>31</sup> Stoeckel).<sup>32</sup>

Lewin<sup>33</sup> holds that all the symptoms, line on gums, ulceration, malaise, diarrhea, nephritis, collapse, are produced by metallic bismuth and have nothing in common with nitrite poisoning. He says that only a marked and easily demonstrable presence during life of methemaglobin in the blood can cause illness or death. All the preparations of bismuth are toxic.

Dalché and Villejean<sup>34</sup> called attention to the similarity in the toxic effects of lead, mercury, and bismuth. It is generally believed that a lead line on the gums is a sign of poisoning by lead; that spongy gums, stomatitis, and salivation indicate poisoning by mercury, then why do not a violet-black line on the gums, salivation and ulceration indicate poisoning by bismuth? It may be, and probably is, true that in certain cases of so-called bismuth poisoning following the administration of enormous single doses of bismuth subnitrate when there was inflammatory disease of the digestive tract, and when there was methemaglobinemia and death, the poisoning was due to nitrites. There is too much experimental and clinical evidence showing that it is the bismuth itself which is the poisonous agent, to allow us to accept unreservedly the idea that all the symptoms in all the fatal cases are due to nitrite poisoning. All the fatal cases reported in which methemaglobinemia was present occurred either in weakly infants the subjects of gastro-intestinal disorders, or in adults in whom there was inflammatory disease of the digestive tract.

A substance which is capable of causing the appearance of albumin and casts in the urine and which experimentally has produced glomerulonephritis, cannot be innocuous.

<sup>24</sup> Loc. cit.

<sup>25</sup> Loc. cit.

<sup>27</sup> Loc. cit.

<sup>29</sup> Berlin. klin. Woch., 1892, p. 1024.

<sup>31</sup> Schweizer Correspondenzbl., 1897, p. 187.

<sup>33</sup> Münch. med. Woch., 1909, lvi, 643 to 645.

<sup>26</sup> Loc. cit.

<sup>28</sup> Loc. cit.

<sup>30</sup> Ibid., 1891, p. 1201.

<sup>32</sup> Quoted by Dreesmann.

<sup>34</sup> Loc. cit.

GENERAL COMMENT. In the literature there are reports of more than 20 deaths caused by the administrations of bismuth preparations internally or as dressings for large raw wounds (burns particularly). There are numbers of cases of moderately severe poisoning such as the case reported in this paper. Verbal and written communications to me show that there must be many cases of rather severe poisoning following the use of Beck's paste which are not reported in the literature.

Beck naturally defends his paste, and in several articles has stated his conviction that the toxic effects are the result of nitrite poisoning. His position does not seem to be tenable in view of the weight of evidence that bismuth itself is at times quite toxic to the human organism.

It seems to be established from the data collected that the indiscriminate use of bismuth subnitrate in sinuses or in the intestinal canal is not devoid of danger. It would appear that one should take care that the paste in sinuses is gradually extruded. Should it remain deep in the sinus, it should be removed after a few days. In using it for x-ray work in the intestines, it appears best to withhold it in inflammatory cases or in cases where patients are much run down in health.

Substitutes such as carbonate of bismuth and oxide of iron,  $\text{Fe}_2\text{O}_3$ , have been recommended and are now being extensively used. The latter is highly recommended (Alexander,<sup>35</sup> Taege,<sup>36</sup> etc.).

In conclusion, it would seem that bismuth salts, like lead and mercury salts, may cause definite and characteristic symptoms of poisoning in more or less susceptible persons. Peculiarly characteristic of bismuth stomatitis is the whitish diphtheritic membrane which caps the ulcers. The visceral lesions caused by bismuth also show that it is one of the metallic poisons and therefore, should be used with caution.

#### ADDITIONAL REFERENCES

- Martens. *Deutsch. med. Woch.*, 1909, xxxv, 1770.  
 Prior. *Münch. Med. Woch.*, 1907, liv, 1934.  
 Bensaude et Agasse-Lafont. *Bull. et Mém. Soc. Méd. d. Hôp. de Paris*, 1909, 3, s., xxvi, 96 to 112.  
 Devic. *Lyon méd.*, 1909, cxlii, 520 to 522.  
 Eggenberger. *H. Zentralbl. f. Chir.*, 1908, xxxv, 1309 and 1537.  
 Dreesmann. *Berlin. klin. Woch.*, 1901, xxxviii, 924.  
 Camerer, C. E. *U. S. Nav. Med. Bull.*, January, 1911.  
 Lawson, G. B. *Southern Med. Jour.*, 1910, iii, 554.  
 Matsuoka, M. *Deutsch. Zeitsch. f. Chir.*, 1910, cii, 508.  
 Ely. *Med. Record*, 1912, lxxxi, 120.

<sup>35</sup> *Deutsch. med. Woch.*, 1909, xxxv, 877.

<sup>36</sup> *Münch. med. Woch.*, 1909, lvi, 1184 and 758.

WEIGHT CURVES IN TYPHOID FEVER.<sup>1</sup>

BY WARREN COLEMAN, M.D.,

PROFESSOR OF CLINICAL MEDICINE AND APPLIED PHARMACOLOGY, CORNELL UNIVERSITY  
MEDICAL COLLEGE; VISITING PHYSICIAN TO BELLEVUE HOSPITAL,  
NEW YORK CITY.

WHILE there can be little doubt that under the ancient doctrine of "stuff a cold and starve a fever," loss of weight in the continued fevers was even greater than it is today, I shall confine the present discussion to the period during which typhoid fever has been recognized as a distinct disease—that is since 1837, when Gerhard and Pennock<sup>2</sup> finally established its differentiation from typhus fever. From that time to the present emaciation has been considered a characteristic symptom of the disease. It occurs in greater or less degree in all or nearly all cases. It is prominently mentioned in all complete descriptions of the disease, and has been regarded as a deplorable but necessary consequence of the infection. According to Loomis:<sup>3</sup> "Emaciation is perhaps more marked and rapid in this than in any other form of fever. It commences early and is progressive. By the time a patient has reached the fourth week of a typhoid of even moderate severity, he is usually in a condition of extreme emaciation." On the other hand, while admitting the occurrence of extreme grades of emaciation, Curschmann thinks that the losses in typhoid fever are not so great as would be anticipated, if one considers the duration of the disease and the extent of the losses in other infections.

Comparatively early in the history of typhoid fever exact observations were made upon the extent of the loss in weight. Yet in view of the fact that the majority of authors do not record the amount of food taken, it is difficult to compare their results. In a few instances, however, they have either plotted out the weight curves or have furnished data from which such curves could be constructed.

The following general summary represents, I believe, the most important results of all previous investigations:

Loss of weight occurs in practically all cases of typhoid fever but varies greatly in extent.

The severer the infection and the longer the duration of the disease, the greater the total loss.

The greatest loss observed by Curschmann<sup>4</sup> at the beginning of convalescence was 41 per cent. of the body weight. Scharlau<sup>5</sup>

<sup>1</sup> Presented in abstract before the Association of American Physicians at the Twenty seventh Annual Meeting, held at Atlantic City, May 15, 1912.

<sup>2</sup> AMER. JOUR. MED. SCI., 1837, xix and xx.

<sup>3</sup> Practical Medicine, 1892, 8th ed., 670.

<sup>4</sup> Nothnagel's Encyclopedia of Practical Medicine, 1905, Amer. ed., 368.

<sup>5</sup> Theoretisch-practische Abhandl. über den Typhus, etc. 1853.

had previously recorded a loss of 30 per cent. Losses of 19 per cent. in severe, and 10 per cent in mild, cases are common (Curschmann). On the other hand, the losses may be relatively insignificant, 1.5 per cent. to 3 per cent. in severe and 1 per cent. to 1.1 per cent. in mild cases (Curschmann.)

Daily losses of 300 to 500 grams are common; they may reach 1500 grams (Botkin<sup>6</sup>); and in a case complicated by parotiditis the loss amounted to 2500 grams in one day (Lorain<sup>7</sup>).

Lorain states that the maximum loss is reached at the end of the second or beginning of the third week, while according to Curschmann it is reached more frequently in the third than in the second week.

Kohlschütter<sup>8</sup> found that, after the more active period of the disease is over, the losses diminish with each week up to complete defervescence. Puritz<sup>9</sup> observed a corresponding diminution in the elimination of nitrogen.

Complications increase the loss of weight (Lorain, Cohin<sup>10</sup>).

While loss of weight usually ends with the return of the temperature to normal, it may extend far into convalescence (Leyden<sup>11</sup>), according to Curschmann to the third week. Curschmann has observed a loss of four pounds in the first week of convalescence.

All patients gain weight in convalescence, some rapidly, apparently without much, if any, increase in the quantity of food.

Contrary to the conclusions of the majority of observers, Garnier and Sabaréanu<sup>12</sup> found in their cases that the weight remained stationary, or increased a little, during the active febrile period; it diminished rapidly at defervescence; and in the afebrile period, remained unchanged until the patient began to take more food, when it increased. They attribute the course of the curve to the retention of water, and its sudden elimination.

Figs. 1 and 2 are taken from Puritz and Lorain. They illustrate the main features of the summary. Puritz's patient received a relatively full diet, taking an average of 160 grams of protein, 60 to 90 grams of fat, and 300 grams of carbohydrate a day. Lorain's patient received only a few spoonfuls of milk.

The loss of weight in typhoid fever has been attributed to three factors: (1) Partial starvation; (2) the febrile temperature; and (3) the toxic destruction of protein.

1. *Partial Starvation.* Apparently at all periods in the history of typhoid fever it has been recognized that patients suffering

<sup>6</sup> Med. Klin. in demonstrativen Vortragen, Berlin, 1867, French translation, Paris, 1872, de la fièvre.

<sup>7</sup> De la temp. du corps humain et ses variations, etc., Paris, 1877-79 ii, 128 et seq.

<sup>8</sup> Volkmann's Sammlung inn. Med., 1887, No. 103 (No 303), p. 2773.

<sup>9</sup> Virchow's Arch. f. path. Anat., 1893 cxxxi, 327.

<sup>10</sup> Bull. gén. d. ther., 1887, cxii, 397.

<sup>11</sup> Deutsch. Arch. f. klin. Med., 1869, v, 366.

<sup>12</sup> Bull. Méd., 1903, xxii, 999.



from the disease were undernourished. Bretonneau<sup>13</sup> characterized their condition by the term *autophagia*. Graves,<sup>14</sup> Trousseau,<sup>15</sup> Chudnowsky,<sup>16</sup> Flint,<sup>17</sup> Barrs,<sup>18</sup> and Shattuck<sup>19</sup> insisted, in their respective periods, that typhoid fever patients were undernourished, and introduced diets of greater nutritive value.

Proof of the influence of partial starvation upon the loss of weight occurring during the disease is furnished by the observations of Puritz, von Leyden and Klemperer,<sup>20</sup> and others who succeeded in diminishing the loss by increasing the intake of food. Recently it has been found possible to maintain many patients in weight equilibrium by administering sufficient food.

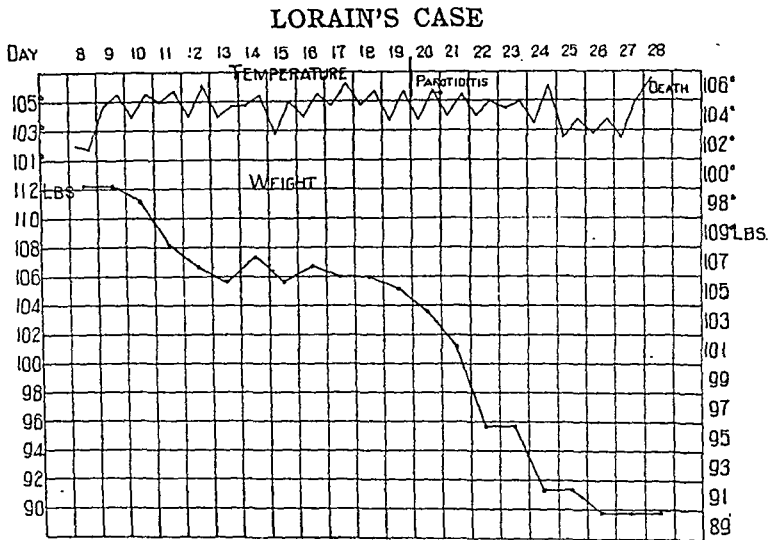


FIG. 1.—Showing influence of complication on weight. Patient received only a few spoonfuls of milk a day.

2. *The Febrile Temperature.* The effects of an artificially raised temperature (through hot baths, heated air, or injury to the heat centres) upon protein metabolism are comparatively well known. It is probable, but has not been proved, that fat and carbohydrate metabolism are similarly affected. Temperatures under 39° C. cause only slight increase in protein destruction; temperatures over 39° C. likewise have but little effect unless they are prolonged for more than three hours; artificial heating for twelve hours has caused an increase in protein destruction amounting to 37 per cent. (F. Voit).<sup>21</sup>

These results apparently confirm the clinical observation that intermittent temperatures are not, as a rule, attended by such

<sup>13</sup> Cited by Trousseau, *Clinique Médicale*, Paris, 1872, 4th ed., i, 353.

<sup>14</sup> *Clinical Medicine*, New Sydenham Society, 1884, i, 136.

<sup>15</sup> *Clinique Médicale*, Paris, 1873, 4th ed., i, 350.

<sup>17</sup> *Practice of Medicine*.

<sup>19</sup> *Jour. Amer. Med. Assoc.*, 1897, xxix, 51.

<sup>20</sup> *Von Leyden's Handb. d. Ernährungs-Therapie*, 1904, 2d ed., p. 332 et seq.

<sup>21</sup> *Sitzungsberichte d. Gesellschaft f. Morph. u. Physiologie in München*, 1895, xi, 120.

<sup>16</sup> Cited by Puritz.

<sup>18</sup> *British Med. Jour.*, 1897, i, 125.

marked loss of weight as those which are continuous. They also suggest that the diminished loss in the later stages of typhoid

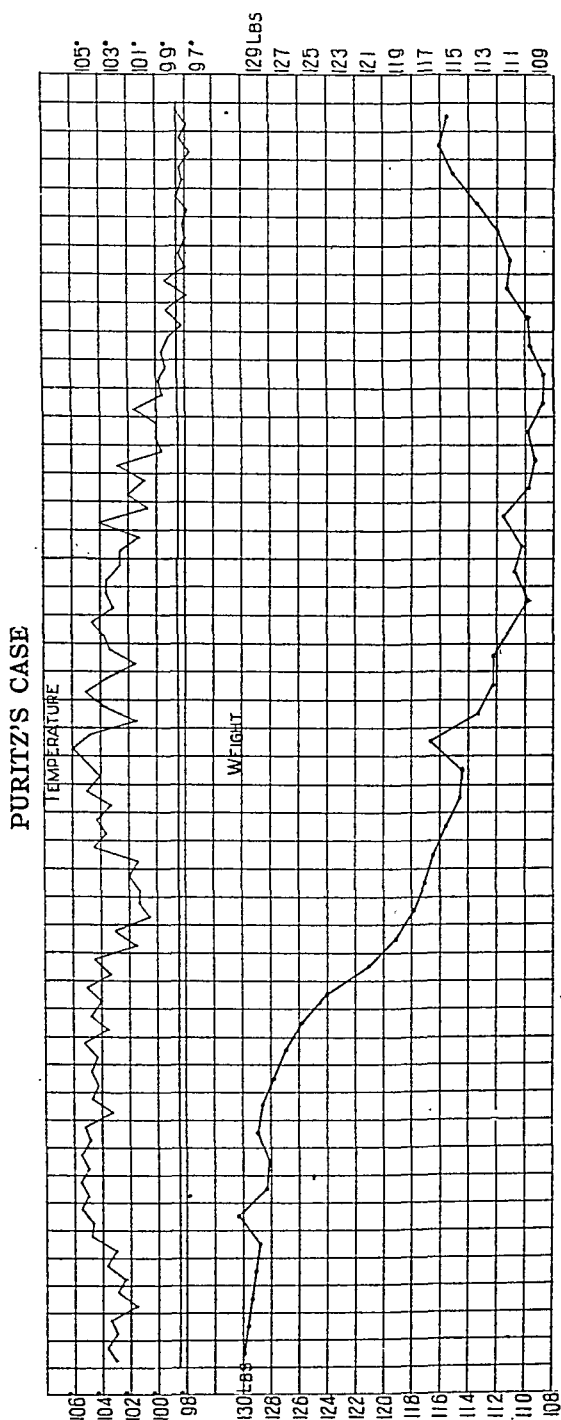


FIG. 2.—Patient received an average of 2600 calories a day.

fever may be due in part to the change in character of the temperature curve.

3. *Toxic Destruction of Protein.* The loss of nitrogen in the infective fevers is greater than occurs in a healthy man who is starved, or, according to the common belief, than can be accounted for by the pyrexia itself. Upon this basis it has been assumed that the toxins of the infecting microorganism exert directly a destructive influence upon the cells of the body.

Whether the theory, in its generally accepted form, is correct or not does not concern us at this time. It has been proved possible to bring a patient suffering from typhoid fever into nitrogen and weight equilibrium by the exhibition of a diet containing a large amount of carbohydrate, and a relatively small amount of protein.

**WATER-RETENTION THEORY.** The discussion of weight curves in typhoid fever would not be complete without reference to the theory of water retention. This theory must be considered from two standpoints: (1) The influence of the disease itself, and (2) the influence of a diet containing a large amount of carbohydrate.

1. *The Influence of the Disease.* The water balance has not been thoroughly investigated for any fever, and conflicting opinions are held concerning it in typhoid fever.

Leyden was one of the first to refer to the theory of water retention. The sudden losses of weight which have been observed with remissions of temperature, especially toward the end of the febrile period, probably indicate that water is retained in some cases. Yet Krauss<sup>22</sup> speaks of the "alleged retention of water in fever" as pure "conjecture." Stähelin's<sup>23</sup> dog, infected with surra, eliminated more water than he ingested. Schwenkenbecher and Inagaki<sup>24</sup> conclude from their experiments that water is not retained in the body in fever,

On the other hand, Garnier and Sabaréanu<sup>25</sup> believe that retention of water occurs during the febrile stage of typhoid fever and that this is responsible for the supposed maintenance of weight during this period.

In view of the conflicting opinions and the absence of conclusive studies of the water balance, the question of water retention in fever due to the disease itself must be left open for the present.

2. *The Influence of a Diet Rich in Carbohydrate.* The increasing use of diets rich in carbohydrate in typhoid fever renders it important to determine whether such a diet is likely to cause retention of water in the body. As is well known, a poorly balanced diet may cause variations in the excretion of water. For example, in an experiment conducted by Benedict and Milner,<sup>26</sup> it was found that water was retained on the first of three days when the subject was confined to a diet consisting of 965 to 969 grams of carbo-

<sup>22</sup> Von Noorden's *Metabolism and Practical Medicine*, Chicago, 1907, ii, 139.

<sup>23</sup> *Arch. f. Hygiene*, 1904, i, 77.

<sup>24</sup> *Arch. f. Exp. Path. u. Pharm.*, 1906, liv, 168.

<sup>25</sup> United States Department of Agriculture, Experimental Stations Bulletin, No. 175, 1903-4, p. 226.

<sup>26</sup> *Loc. cit.*

hydrate; on a diet of 745 to 750 grams of fat, water was lost during the whole period. It is generally agreed, however, that a well proportioned diet does not affect the water balance.

While the proportion of the foodstuffs in the diet which we employ varies necessarily with different patients, and in some instances has been subject to sudden experimental changes, there has been no constant relation between variation in weight and the quantity of urine. Though water may have been retained by some patients, and have caused an increase in weight, there has been no clinical reason to think that such was the case. There has been no visible edema, and patients have not lost weight suddenly, following diuresis, when the amount of carbohydrate in the diet was diminished during convalescence.

In addition to the above considerations, we now possess evidence that at least a part of the gain in weight in the late stage of the febrile period and in convalescence is due to the conversion of dextrose into fat. In one instance, 38 per cent. of the carbohydrate metabolized during the period of observation (fifteen minutes) was so transformed.<sup>27</sup>

*The distribution of the losses* among the various tissues of the body requires brief consideration.

It appears probable that all of the tissues share in the losses, though to what relative extents can only be surmised at present. The increased elimination of nitrogen in patients who are undernourished, forms the basis for the assumption that the muscles suffer marked loss. Loss of fat, as well as of muscle, is evident clinically in severe cases.

With the aid of a respiration chamber, Grafe<sup>28</sup> studied the respiratory quotients of typhoid fever patients in the fasting state, and reached the conclusion that the metabolic processes follow normal laws, though with increased intensity. Rolly's<sup>29</sup> studies on the respiratory quotients of patients from four to six hours after food, and our own studies in Bellevue Hospital upon patients taking a full diet, lead to the same conclusion. If these results are ultimately confirmed, the consumption of the body tissues in typhoid fever, when the patients are undernourished, proceeds in the same manner as in healthy persons who are partially or completely starved. The stores of glycogen are depleted first—probably within a few hours when the fever is high and, at most, within a few days—after which fat and protein constitute the sole sources of the body's energy. The duration of life in a healthy animal which is starved is measured by the amount of fat which the body contained at the start (Lusk).<sup>30</sup> The often noted fact

<sup>27</sup> Unpublished observations upon the respiratory exchanges carried out with the assistance of Dr. E. F. Du Bois.

<sup>28</sup> Deutsch. Arch. f. klin. Med., 1910, ci, 209.

<sup>29</sup> Ibid., 1911, ciii, 93.

<sup>30</sup> Science of Nutrition, 1906, p. 65.

that obese patients do not bear typhoid fever well does not come into consideration here, since the causes of this fact can only be conjectured. Another analogy of the processes of metabolism in typhoid fever to those in starvation must be noted: in partial or complete starvation the body begins, after a time, to economize its available energy by reducing its total metabolism. A similar economy of energy has frequently been observed in typhoid fever. Moos<sup>31</sup> found as long ago as 1855 that the nitrogen losses diminished in the later weeks of the disease. Kohlschütter<sup>32</sup> emphasized his observations that the loss of weight diminishes with each week after the more active period of the disease is past. Cohin<sup>33</sup> called attention to the same fact. This is the probable explanation of the continuance of life in patients who take a wholly inadequate amount of food and yet live from week to week with high fever.

**INFLUENCE OF THE HIGH-CALORY DIET UPON WEIGHT.** My own observations upon the weight curve in typhoid fever were begun in 1908. A satisfactory balance could not be obtained upon the market so I had the hospital carpenter construct a wooden table which would rest upon the platform of the ordinary hospital scales. When in position, the table is the same height as the bed, and the weight of a patient may be taken without more disturbance than shifting his position in bed—with much less exertion, in fact, than is required to administer a tub bath.

Weights have been taken of practically all patients, usually every second or third day. The procedure was adopted originally for the purpose of having additional clinical control upon the effects of the diet. Slight sources of error enter into the observations, which are clearly recognized, but which so far it has been impossible to eliminate.<sup>34</sup> While such errors may, and probably do, affect the relation of one day's weight to another, apparently they do not affect the general trend of the curve. The errors referred to are: Patients have not always been weighed at the same hour of the day, or with regard to whether they have recently been fed or have urinated. The morning defecations do not come into consideration as the weights have never been taken before the administration of the daily enema. The clothing of the patients, however, has always been carefully considered. In future observations, it is hoped that these sources of error may be eliminated.

The figures which follow, with the exception of Fig. 3, illustrate the influence of a full diet upon the weights of patients during the febrile period, convalescence, and relapses. The curves are typical of the effects of the diet. Fig. 3 is the curve of one of the earlier patients of the series, to whom it was impossible, with our

<sup>31</sup> *Zeitschr. f. rationelle Med.*, N. F., No. 7, 1855.

<sup>32</sup> *Loc. cit.*

<sup>33</sup> *Loc. cit.*  
<sup>34</sup> The weights have been taken by various members of the interne staff after the general demands of the wards have been attended to.



then limited experience, to give the amount of food required until toward the end of the febrile stage. The general course of the curve is similar to those obtained by the earlier investigators.

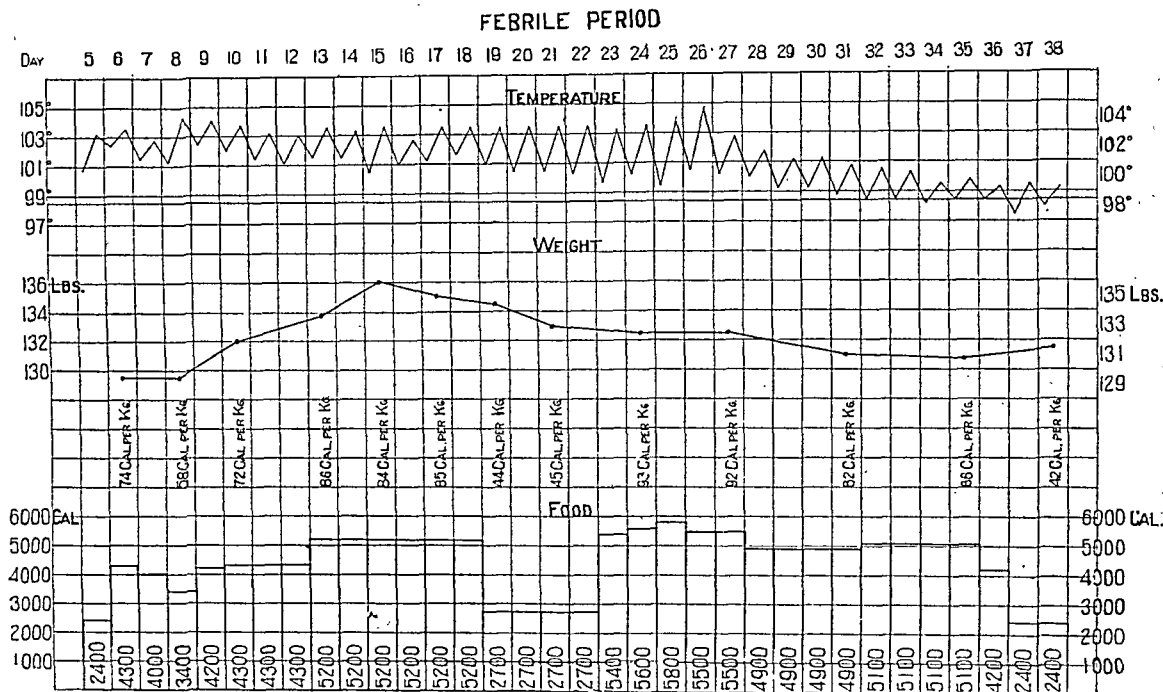


FIG. 4.—Showing that weight equilibrium may be maintained by sufficient food.

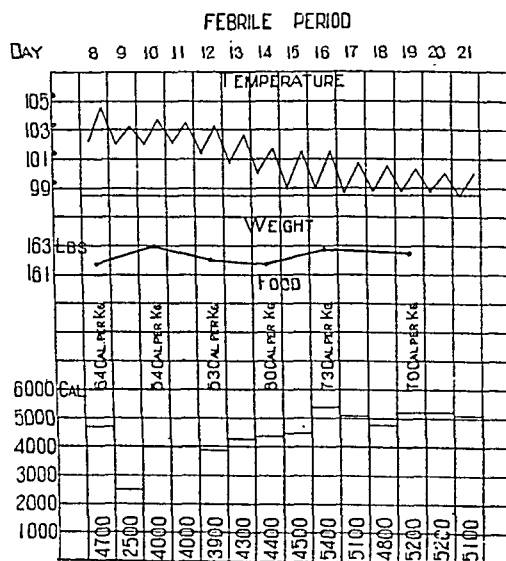


FIG. 5.—Showing the maintenance of weight equilibrium.

There is no evidence in the curve of water retention either during the febrile period or in convalescence.

The gains in weight during relapses and in convalescence are

less noteworthy than the maintenance of weight during the active stages of the fever.

The ability of the body to repair its losses after wasting diseases is nowhere better shown than in convalescence from typhoid fever. This fact has been known for many years. Botkin stated that such patients gained weight rapidly at first, more slowly later. According to Liebermeister,<sup>35</sup> patients may gain as much as five to seven pounds a week, according to Schottmüller,<sup>36</sup> as much as eleven pounds. In Puritz's cases, the weight remained stationary for the first two or three days after the temperature reached normal and then began to increase. Fr. Müller<sup>37</sup> found that patients convalescing from typhoid fever are able to retain nitrogen on a diet which

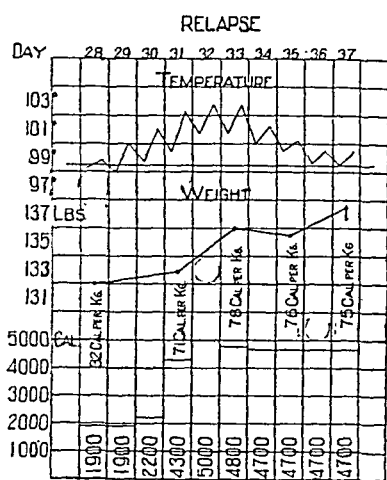


FIG. 6.—Showing an increase in weight during a relapse.

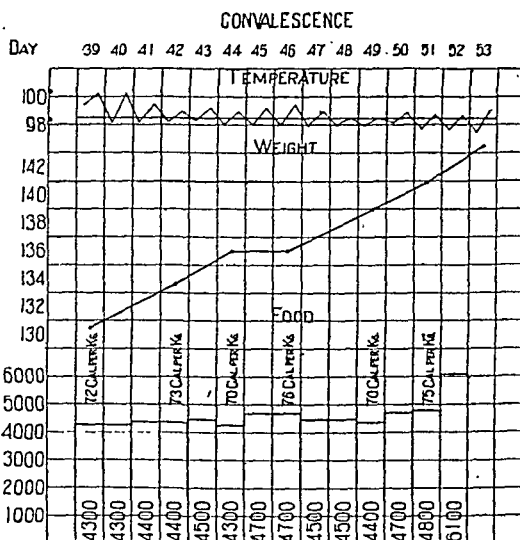


FIG. 7.—Showing rapid gain in weight during convalescence.

with its low fuel value is insufficient to maintain nitrogen equilibrium in health. He reports a case which retained from the third to the tenth day of convalescence a daily average of 1.3 grams of nitrogen on a diet furnishing only 1165 calories and 9.9 grams of food nitrogen.

As is illustrated in Fig. 3, patients who have lost much weight during the febrile stage may repair the damage before they are able to get out of bed.

In one of Puritz's cases the weight remained stationary during a relapse of sixteen days' duration.

**CONCLUSION.** It is possible to maintain patients suffering from typhoid fever in weight equilibrium throughout the entire course of the disease by giving them sufficient food.

<sup>35</sup> Ziemssen's Cyclopaedia of the Practice of Medicine, Wood, 1874, i, 95.

<sup>36</sup> Mohr and Stähelin's Handb. d. inn. Med., 1911, i, 483.

<sup>37</sup> Zeitschr. f. klin. Med., 1889, xvi, 542.



# OBSERVATIONS UPON SCARLET FEVER, DIPHTHERIA, AND MEASLES AT THE CINCINNATI CONTAGIOUS HOSPITAL.

BY ALBERT J. BELL, A.B., M.D.,

VISITING STAFF, CONTAGIOUS GROUP, CINCINNATI HOSPITAL

ALTHOUGH there are numbers of good men who, patiently and perseveringly, are working in their laboratories and wards upon the problems which our contagious diseases present, and the results of their efforts appear at intervals, one is impressed with the comparatively little written upon the subject. I refer in this paper only to scarlet fever, diphtheria, and measles. This may be due to a placid conclusion on the part of many that our text-books have settled the clinical signs and symptoms and that repeated failures along etiological and bacteriological lines yield little of promise for the future. This I think is incorrect and some one's persistent efforts will eventually be crowned with success.

Scarlet fever appears variously disguised, probably more so than any other contagious disease, and if we can find out practically for ourselves that we have in the past laid too much stress upon certain so-called classical signs and not enough upon others and that a rearrangement of some of our ideas seems advisable, we may be helped to an earlier recognition and, therefore, a more prompt isolation and treatment of this affection. During the last year in the contagious hospital we have had an excellent opportunity for studying this disease especially, and it is my desire to furnish statistics as we found them in this and the other diseases, with certain observations which were made concerning clinical manifestations, laboratory findings, and treatment.

Observations were made upon over 300 cases of scarlet fever. The following summary indicates in percentage form our findings in the so-called classical symptoms and diagnostic signs:

Scarlet fever, 315 cases. Onset with vomiting, 50 per cent.; onset with headache, 4 per cent.; onset with sore throat, 65 per cent.; eruption, whole body, 46 per cent.; eruption, partial, 35 per cent.; mouth pallor, 57 per cent.; rash on soft palate, 38.6 per cent.; membrane on tonsils, 29 per cent.; papillæ enlarged, 56 per cent.; glazed tongue, 17.7 per cent.; anterior cervical glands enlarged, 95 per cent.; submaxillary glands enlarged, 72 per cent.; eruption gone from body, five and one-half days; desquamation began in six and three-quarter days; blood count, leukocytes average, 17,000; polymorphonuclears, average, 78 per cent.; large lymphocytes, average, 6.3 per cent.; small lymphocytes, average, 10.1 per cent.; eosinophiles, average, 2 per cent.; albumin, 11 per cent.; granular casts, 4 per cent.; hyaline casts, 2.5 per cent.; blood cells, 4 per cent.; myocarditis, 6 per cent.; irregular heart,

3 per cent.; murmurs, 8 per cent.; mastoiditis (no facial palsy in this series), 1 per cent.; arthralgia (all cases had immunizing doses of diphtheria antitoxin), 6 per cent.; acetone, 49.5 per cent.; diacetic acid, 22.6 per cent.; indican, 73 per cent.; temperature gone in five and two-third days; nephritis, 2 per cent. The average white count of cases which died was 17,262. Preponderance of the staphylococcus may have influenced all leukocyte counts.

Concerning the above summary a few comments seem pertinent: Onset with vomiting occurred in only 50 per cent. of our cases which is rather disappointing, as so much stress has always been laid upon this sign. McCullom<sup>1</sup> says that it occurred in 80 per cent. of his cases, but Welch and Schamberg give their figures also as 50 per cent., and add that they consider this rather lower than usual. I think that this is a just criticism and that in most epidemics the figures would be considerably higher.

We observed mouth pallor in 57 per cent. which is also lower than we would expect. No statistics were obtainable from other sources in regard to this, McCullom merely says that it occurs constantly in moderately severe cases. It has been our experience that the rash occurs on the face in only a small number of the cases, but when this is present or if there is only a febrile blush upon the cheeks, the skin around the mouth and nose remains exempt. When this is seen I believe it to be quite characteristic.

Thirty-eight and six-tenths per cent. had rashes upon the soft palate and fauces and where this is present, namely, a generalized blush, punctate in character, I believe it to be our most important diagnostic sign.

The papillæ appeared enlarged in 56 per cent. of our cases. Concerning this McCullom says that the condition is constant, but may be missed at times, and Welch and Schamberg say that it may or may not be present in mild cases. When present, even with the glazed tongue (17.7 per cent.), it is not absolutely pathognomonic, as it may occur in certain forms of gastro-intestinal disturbance in which there is not the slightest suspicion of scarlet fever. The strawberry tongue, however, taken together with a generalized blush, punctate in character, upon the soft palate and fauces, need leave very little doubt as to the character of the disease.

I think these two symptoms are very much more significant than an apparently characteristic rash upon the body. We have tried to emphasize the importance of laying more stress upon the mouth symptoms and not depending upon the body rash. However, the whole picture should be considered.

Our average white count was 17,000. The maximum was 38,000. The text-books lead us to expect a uniformly higher count than

<sup>1</sup> Osler's Modern Medicine;

this. We felt that a satisfactory one was between 20,000 and 35,000. Kotschetskoff and Bowi's<sup>2</sup> figures are between 10,000 and 40,000, Rieder's 40,000, Felsenthal between 18,000 and 30,000, and Tileston between 18,000 and 40,000.

The average polymorphonuclear count was 78 per cent. Kotschetskoff gives between 85 and 98 per cent.

The low percentage of eosinophiles, 2 per cent., was probably due to the fact that the blood counts were made early in the disease.

McCullom observed albumin in 72 per cent. of his cases at the South Department, while Roger reports 38 per cent. Our cases showed the presence of albumin in only 11 per cent. I believe that a practical reason for this may be found in our routine treatment. All cases were confined to bed for at least three weeks and kept upon a strictly milk diet until their temperatures were normal for seven days. Eggs and broths were withheld until the fifth week and red meats until the latter part of the sixth. Of equal importance with this is the systematic giving of large quantities of water from the time of their admission to the hospital. At first potassium citrate was ordered, more or less as a placebo, to be given hourly or two hourly in water, with the idea that the patients would get the fluid more religiously if medicine were ordered with it. How much restraining influence the alkalinizing power of this drug exerted upon the presence or absence of albumin in the urine we will consider later.

In our estimate of nephritis we included all cases showing the presence of albumin, casts, and red blood cells, and this we found to be only 2 per cent. Welch and Schamberg<sup>3</sup> quote Vogl as reporting 34 per cent. of nephritis in his cases, Cadet de Gassicourt, 30 per cent., Baginsky, 9.57 per cent., Caiger, 3.32 per cent., and Holt gives as his figures between 6 and 10 per cent.

Let me call attention to the fact that about 50 per cent. showed the presence of acetone in the urine; less than half that number showed diacetic acid, and almost 75 per cent. reacted for indican.

Practically all the cases desquamated, although some very slightly.

None of our scarlet fever cases contracted diphtheria in the house, although 2 or 3 showed the presence of the Klebs-Loeffler bacillus upon admission. The most susceptible period for this disease is the third, fourth, and fifth week. Variat and Deve report 30 cases positive for the Klebs-Loeffler bacillus in 525 scarlet fever patients; Garret and Washburn,<sup>4</sup> London Fever Hospital, report 1 per cent.; Welch and Schamberg,<sup>5</sup> Municipal Hospital in Philadelphia, found between 19 and 32 per cent. positive. Some allowance should be made for the method employed

<sup>2</sup> Quoted by Welch and Schamberg.

<sup>4</sup> Ibid.

<sup>3</sup> Ibid.

<sup>5</sup> Ibid.

in reporting the presence or absence of the Klebs-Loeffler. We used the Westbrook classification entirely, which is liberal and will be referred to under diphtheria. At least four cultures were taken from the noses and throats of all scarlet fever patients.

The so-called Pastias sign in this disease, namely, the accentuation of the rash in the normal folds, especially on the anterior surface of the elbow, has not been noticed except in a few instances, so that no significance has been attached to it.

Of like importance is the Rumpel-Leeds phenomenon or the hemorrhages at the elbow from compression of the upper arm by means of a bandage. Observations made by others have shown it to occur with equal frequency in measles and in normal children.

In taking up the treatment of special conditions we may first refer briefly to the subject of immunization against scarlet fever. We have had practically no personal experience with this line of work, except to give one light case which was exposed to the most virulent form of the disease one million killed streptococci taken from scarlet fever patients (a vaccine which was on the market) and which case continued to have a mild attack, and another, a very malignant case, five daily doses from 500,000 to 4,000,000 of the same scarlet fever vaccine. This patient's condition was uninfluenced by the treatment and the patient died in a few days. The above should come under the heading of treatment of the disease rather than immunization. If there is any close connection between the streptococcus and the virus of scarlet fever we would look for our best results from an antistreptococcus serum, made from scarlet fever patients rather than a vaccine, as the former (the serum) already contains the antibodies and should act more promptly, while the latter (the vaccine) simply helps the patient to form his own. The field for the vaccine is in immunization.

With the use of the ordinary antistreptococcic serum made up of streptococci not from scarlet fever patients we have noticed little benefit even in doses of 80 or 90 c.c. in twenty-four or thirty-six hours. If it is used at all it should be made from the streptococci from blood, throat, or glands of scarlet fever cases. Such a serum has been hard for us to obtain from any source, because of the difficulty we have experienced in isolating streptococci from our cases.

Federinski in Moscow (1910), in an analysis of 317 cases which received the antistreptococcic serum (made from scarlet fever streptococci) says that it helps chances of recovery if given before the fifth day. His dosage was 200 c.c. to adults and 100 to 150 c.c. to children, repeated in twenty-four or forty-eight hours if necessary. Mathias Nicoll, New York (1910), reports only fair results. If obtainable, it should be used in some cases, in enormous doses always, for lack of something better, either subcutaneously

or intravenously, according to immediate needs. It might help minimize the complications.

Professor Schwenkenbecker, director of the Frankfurt Hospital Medical Clinic, recommends the injection intravenously, not later than the fourth day, of serum (healthy as to syphilis or tuberculosis and culturally sterile), taken from at least 3 (namely, a polyvalent serum) scarlet fever cases suffering from a severe but uncomplicated type of the disease in late convalescence. Treatment with this sera should cease not later than the eighteenth to the twenty-fourth day from the onset. The dose should be 40 c.c. for children and 100 c.c. for adults, and doses may be given at intervals of from one to seven days according to the severity of the case. He suggests that only the severe and unquestioned cases of scarlet fever be injected.

Karl K. Koessler and Jessie M. Koessler,<sup>6</sup> in experiments concerning specific antibodies in scarlet fever concluded that "the serum of scarlet fever patients contains specific antibodies for an unknown virus which seems to be present especially in the cervical lymph glands." Personally, I think that we should direct our efforts toward discovering a specific serum for the treatment of this disease to the preparation of sera derived from the blood stream or, more probably, from the cervical lymph glands of scarlet fever patients, rather than to vaccines or serums containing the streptococcus or its antibodies.

Out of 50 or more nurses who have been on duty in the wards, 3 (about 6 per cent.) contracted the disease in the house, while none of the internes did.

W. H. Waters, of Boston, reports results in immunization against scarlet fever, of nurses on contagious duty. He used different strains of streptococci, killed and standardized in usual way, taken from throats of scarlet fever patients. For two or three weeks before going on duty the nurses received three immunizing doses, of 50,000,000, 100,000,000, and 200,000,000 organisms of a polyvalent vaccine. Of those receiving the vaccine, 2.7 per cent. contracted the disease and of those not receiving it 35.7 per cent. contracted it. These figures are rather amazing as his nurses must have been unusually susceptible.

Kolmer, of Philadelphia, in trying to raise the streptococcoson index, found experimentally that he was able to do so slightly, but concluded that it was so slight as to make the likelihood of establishing an immunity against streptococcic infection very dubious. Again, in experimental studies on streptococcus antibodies with special reference to complement fixation reactions, he concludes that a streptococcus produces a specific antibody up to a certain limit, but "finding but 11.2 per cent. of positive

<sup>6</sup> Jour. Infect. Dis., November, 1911, vol. ix, No. 3.

reactions in scarlet fever tends to show that streptococcus infection in scarlet fever severe enough to produce immune bodies is not so common as is generally believed."

Nasal and ear discharges were reported promptly and a number of autogenous and stock vaccines (in all 10, an inconclusive number it is true) were prepared.

It is the opinion of most workers that stock vaccines give equally as good, if not better results than the autogenous, because the former can be administered much more promptly and several days are gained for the patient, a very important consideration. Our results with these vaccines were not brilliant. Cases using vaccines had no local treatment. Irrigations were employed for the others. Except in one or two instances we could not see that the discharge was in any way modified by the vaccine and on the whole, those having local treatments ran a shorter course. The dosage in each case was started with about 200,000 and each succeeding dose was doubled at intervals of from two to ten days according to indications. This was carried up to 128,000,000 in some cases. This method has so far been disappointing, but in the hands of Kolmer, of Philadelphia, good results have been reported. It is possible that in some instances our intervals of administration and dosage were faulty, yet the method is certainly in line with modern vaccine therapy in other directions. Many cases, however, having local treatments, where intelligently applied, yield results, which, if vaccines were being used, would be considered brilliant.

We have taken the opportunity in our wards of applying wherever feasible, the treatment for nephritis as suggested by Dr. Martin Henry Fischer.<sup>7</sup>

This therapy is based upon certain theories, or more correctly, facts, since they have been confirmed by laboratory experiments and as they are a departure from our formerly accepted views on nephritis, it may be well to briefly summarize a few details of his work and conclusions for the benefit of those who are not familiar with them. They are as follows:

It is assumed that nephritis is due to an acidosis in the kidney. Emphasis is laid upon the colloidal structure of the blood, both red and white corpuscles and the liquid portion, also that the urinary membrane, namely, everything between the urine and the blood, consists of various emulsion colloids in the solid state. Colloid material is also present in the urine normally, but is not visible as albumin to our ordinary tests.

The fluids and tissues of the body (except the gastric juice, urine, sweat, vaginal secretion, and alimentary contents, when fat is fed) are practically neutral in reaction. Normal blood is neutral in reaction, but contains both alkalies and acids.

<sup>7</sup> Nephritis.

An abnormal production or accumulation of acid in the kidney renders the colloidal urinary membrane soluble and permits a part of it to pass into the urine as albumin.

This has been demonstrated by experiments. Fibrin, an albuminous structure, when mixed and shaken with plain water (of neutral reaction) swells only slightly and the water shows no reaction for albumin. If hydrochloric acid is added there is greater swelling of the fibrin and albumin is present (by the precipitation of the fibrin) in the water in accordance with the amount of swelling. If sodium chloride or any other salt is mixed with the hydrochloric acid, less albumin goes into solution, the higher the concentration of the salt. Gelatin (another colloid) acts practically the same way as fibrin.

A high alkali content can as readily put the colloids, fibrin, and gelatin into solution (namely, dissolve the albumin) as can an acid. This is probably no factor in the production of a nephritis as the normal  $\text{CO}_2$  production in the living cells tends quickly to neutralize it.

Fischer found that by injecting acid into the ear of a rabbit, its normally alkaline urine became acid. Albumin, casts, epithelial cells, blood corpuscles, and hemoglobin appeared promptly in the urine which was also diminished in quantity. Edema of the tissues was noticed as well.

An over supply of acid in the tissues in extreme muscular exertion and the severe anemias, without adequate oxidation, shows albumin in the urine.

Contrary to the views of many he holds that albuminuria is the constant accompaniment of salt starvation.

Actual experiments on the kidney by Fischer are in line with the preceding observations. He found that the structures of the kidney in the presence of an acid swell, take in water, and part of the colloid material is dissolved as albumin and precipitated as granules.

This brief summary suggests the "Fischer" treatment for nephritis, namely, an alkali, salt, and plenty of water.

It occurred to us that as the contagious diseases are frequently accompanied by an acidosis, as exemplified by the presence of acetone in about 50 per cent. of our cases and diacetic acid in 22.6 per cent., that the alkaline treatment might help to control the progress in the severe septic types of the disease. Apparently it exerted little or no influence in staying the course of the purely septic types which were unaccompanied by any special nephritis. Fischer says that he would not expect it to have any material influence upon that type of case. Sodium carbonate given by the mouth was not well tolerated as a rule, and seemed to be somewhat more irritating to the rectum than a normal salt solution. However, a large majority of the cases retained a sufficient amount

in that way. Potassium citrate was substituted when giving an alkali by mouth and has been given to all my cases hourly or two hourly, whether or not they had evidences of albumin or nephritis. Probably the low percentage of albuminurias (11 per cent.) and that of nephritis (2 per cent. in 388 cases of scarlet fever) observed in our wards is due to the routine alkaline "plenty of water" treatment, which all the cases have had. Their urine part of the time was alkaline and never highly acid.

Two cases present interesting features:

CASE I.—M. D., male, aged three years. Severe septic type with both ears discharging, profuse nasal discharge, enlarged glands, weak, irregular heart with bruit at apex, eyelids, and feet edematous. Urinalysis, albumin negative. Amount of urine very scanty, blood cells and hyaline casts. Started alkaline-salt solution per rectum. The solution contained sodium carbonate (crystals), 10, sodium chloride, 10, in 1000 c.c. of water. A half strength dilution of the above was used. Four ounces were given per rectum every three hours and were expelled occasionally. Potassium citrate, grains five in water, was given by mouth every one to three hours.

On the ninth day of the illness Fischer's solution was given intravenously. Same formula as above was used except that sodium chloride was increased to 14 in the 1000 c.c. of water and a half dilution given. Only 10 ounces were used as the patient showed signs of collapse. At least a pint and a half should have been given very slowly had we been able to do so. Next day one pint was given again intravenously. The amount of urine passed increased promptly, and the edema disappeared. Gradual improvement of general symptoms with complete recovery resulted.

CASE II.—J. D., male, aged four years. Light case of scarlet fever with temperature reaching normal on the fifth day. He passed from 8 to 33 ounces of urine daily up to the thirty-first day of the illness. On the twenty-seventh day (end of fourth week) the urinalysis showed: Specific gravity, 1010; albumin, a heavy trace; few coarse granular casts; red and white blood cells.

The child was somnolent and was aroused with difficulty. Vomited several times. Pulse varied between 90 and 122, with blood pressure high (systolic pressure sometimes reaching 144). The child seemed on the verge of uremic convulsions. There was puffiness of the face and eyelids and slight edema of the feet. There was no fluid in the serous cavities at any stage.

For thirteen days after the nephritis commenced, except once, albumin from a slight to a heavy trace was reported daily in twenty-four-hour specimens. It then disappeared not to return again.

During the presence of albumin, red and white cells were found in abundance. Casts were rare. An occasional granular, and a few blood casts were reported once and part of one cast another



time. There were no hyaline casts. After eight days the blood cells were few in number and gradually disappeared, to be entirely gone about the eighteenth day. The specific gravity varied between 1002 and 1028, usually between 1002 and 1010. The urine was reported as acid only twice after the fourth day. The amount of urine passed daily varied from 30 to 60 ounces.

**TREATMENT.** The treatment was as follows: For ten days after albumin was discovered the patient had sodium chloride, grains five, and potassium citrate, grains eight, by mouth in as much water as he would take every hour day and night. Fischer's solution, one-half dilution (of the sodium chloride 10, sodium carbonate, crystals, 10, water 1000 c.c. strength), ounces, five, per rectum was given at two hour intervals during the day and three hour intervals during night, and was retained. After ten days the intervals of administration both by mouth and rectum were lengthened.

During the period of high blood pressure, *veratrum viridi*, minims two, every three hours, was given during the day. Fischer's solution intravenously was not necessary.

Blaud's pills were started during convalescence as a tonic. During the attack the child showed a mild grade of anemia. The red blood cells were 4,600,000. Recovery was complete.

There were several interesting features about this case. He started with what appeared to be a terrific case of nephritis with the urine absolutely loaded with red blood cells and a large amount of albumin. One striking thing was the great scarcity of casts of all descriptions. How much this was influenced by keeping the urine absolutely alkaline, by the constant administration of salt, and the ingestion of large quantities of water is an interesting question. With the starting of the treatment all symptoms improved and continued to do so consistently.

We found that grains twelve to thirteen hourly of potassium citrate by mouth in the adult and grains five to seven in children, aged four to seven years, was sufficient to keep the urine alkaline.

As I have said before, nephritis has been of rather rare occurrence in our wards, but whenever tried the alkaline salt treatment has given satisfactory results.

True relapses or reinfections were not observed, but delayed rashes occurred in 1 or 2 instances.

Eighteen blood cultures were made during the year from scarlet fever patients. Of these 9 were negative. In the other 9 cases the *Staphylococcus pyogenes aureus* was recovered seven times and the *albus* twice. We were unable to recover the streptococcus from the blood.

The throat and nose cultures almost uniformly showed the presence of staphylococci, occasionally mixed with a few streptococci.

Atmospheric plate cultures (88 in number) in wards before fumigation showed the presence of the *Staphylococcus aureus* and *albus*, the *Streptococcus pyogenes*, but never the Klebs-Loeffler bacillus. After fumigation with formaldehyde, plate cultures were always negative.

Twelve cervical glands of scarlet fever patients were aspirated with aseptic precautions in an effort to corroborate the claims of Vipond made in the spring of 1911, that he had found the specific organism of scarlet fever in the glands of patients suffering from this disease. The cultures were sterile in 9 cases; the *Staphylococcus pyogenes aureus* was isolated twice and the *pyoscyaneus* once. Our results did not verify his findings. This has also been the experience of others. Experiments by Dr. Nicoll show that Vipond's bacillus was probably a contamination from the asbestos packing of his syringe.

The following summary shows observations made upon 76 cases of diphtheria:

Onset with sore throat, 84 per cent.; onset with vomiting, 33 per cent.; membrane on tonsils, 85 per cent.; membrane on soft palate, 36 per cent.; inflammatory swelling, 30 per cent.; membrane gone on the average in two and seven-elevenths days; temperature normal on the average in three and three-quarter days; erythema (not from serum), 5 per cent.; urticaria (not from serum), 14 per cent.; otitis, 5 per cent.; albumin, 12 per cent.; adenitis, 47 per cent.; paralysis, soft palate, 5 per cent.; paralysis of other muscles, 4 per cent.; myocarditis, 16 per cent.; endocarditis, 28 per cent.; slow pulse, 4 per cent.; arthralgia, 2.6 per cent.; acetone, 28.5 per cent.; diacetic acid, 14 per cent.; indican, 32 per cent.; serum rashes, 16 per cent.; antitoxin, average dose, 40,000 units, highest dose, 355,000 units; blood count: Leukocytes, average, 13,633.

Types of Klebs-Loeffler bacilli found in Wesbrook classification: C, 58 per cent.; D, 39 per cent.; A, 22 per cent.; E, 8 per cent.; E<sub>2</sub> and F<sub>2</sub>, 5 per cent.; B, D<sub>2</sub>, and F<sub>1</sub>, 3 per cent. Other solid forms occurred less frequently.

Glancing at the table we see that vomiting occurred at the onset in only 18 per cent. of the cases while in scarlet fever the percentage was 50.

A striking feature about the table is that the average dose of antitoxin was 40,000 units. This is accounted for by the fact that a number of desperate cases, having been sick about a week before admission, required enormous doses which brought up the average considerably. Many required only small doses. Our rule was to give from 2000 or 3000 to 12,000 units from two to three times in twenty-four hours, until signs of improvement were noticed.

A husband and wife, sick one week before admission, came in completely overwhelmed by the disease. The former had the

pharyngeal type, his pharynx being completely covered by a membrane about one-eighth of an inch thick. He had the record dose, 355,000 units. He developed some arrhythmia, but showed no serum rashes or arthralgia. He was in an advanced stage of tuberculosis before acquiring diphtheria and died from that disease later. His wife had a bad laryngeal type of diphtheria, with pronounced stenosis, loss of voice, and extreme prostration. She received 345,000 units and made a complete recovery, without serum rashes, arthralgia, evidences of myocarditis, or any other complication. Advanced laryngeal cases received antitoxin unsparingly.

Whether or not hospital cases receive more antitoxin than is absolutely necessary, they, at least, cannot be judged by the standard set in private practice where the cases receive treatment promptly.

Our cases show some features which are worth mentioning. The average time for the disappearance of the membrane was two and two-third days and normal temperature averaged three and three-fourth days. Paralysis of the soft palate occurred in only 5 per cent. Other paralysis, 4 per cent. Arthralgia was noticed in only 2.6 per cent. and serum rashes in 16 per cent. Concentrated serum was always used. No anaphylactic phenomena were observed in any of our cases. Our mortality for diphtheria as reported up to January 1, 1912, was  $3\frac{1}{3}$  per cent.; while for scarlet fever it was 6.5 per cent. This is at least an illustration of the principle that large doses of antitoxin need not be feared, and that it neutralizes all the toxin. The converse applies forcibly to insufficient dosage. Promptness in administration is an important guide to the size of the dose.

The Westbrook<sup>8</sup> classification was used routinely in examinations for the Klebs-Loeffler bacillus. A, C, and D, the granular types, were regarded as positive and when found three successive negative cultures were required before discharge.

A<sub>1</sub>, A<sub>2</sub>, B, B<sub>2</sub>, C, C<sub>2</sub>, and E (the barred types except E), were called doubtful, and when found put the patient back for only one culture instead of three. The solid forms were regarded as negligible. This method is a liberal one as it makes a distinction between the virulent and non-virulent types.

No use was made of the Diazo reaction in diphtheria as a differential sign between a purely serum rash and true scarlet or measles. It occurs in 17 per cent. of scarlet fever cases, 12 per cent. of diphtheria, and 75 per cent. of measles cases. In the latter it might be helpful.

Little difficulty was experienced with the persistence of the Klebs-Loeffler bacillus in the throats of convalescing individuals.

<sup>8</sup> Amer. Jour. Public Hygiene, May, 1907.

This happened only two or three times. The early negative findings were undoubtedly influenced by frequent throat irrigations and sometimes nasal, of normal salt solution or bichloride solution (1 to 12,000) or simple applications of the latter (1 to 4000).

L. M. De Witt and others recommend the application and sprays of fresh cultures in broth of the *Staphylococcus pyogenes aureus* for persistent Klebs-Loeffler bacilli in the throat. This should not be done until convalescence, when the mucous membrane presents a normal healed surface. There is no incompatibility between the Klebs-Loeffler and the staphylococcus, but the latter assists in reinforcing the normal throat flora.

Max Crohn<sup>9</sup> recommends small doses of antitoxin (2000 units) subcutaneously for post-diphtheritic paralysis and reports good results. We have not tried it, and should hesitate to do so except in very favorable cases for fear of serum sickness.

Bingel<sup>10</sup> recommends intraspinal injections of diphtheria antitoxin for late cardiac failure after this disease. The condition is so grave that anything which gives even remote promise should be tried.

Cumberland, of England, recommended the use of antitoxin by the mouth. The initial dose was 4000 units, followed up if necessary by 2000 units more. He did not observe serum rashes or joint pains following the use of this method, and obtained results within a few hours after administration.

We tried this with a few cases (5 in number) and selected them with reference to mildness rather than severity of type. It was administered in milk and usually well borne. We used only small doses, but seeing very slow response gave more than he recommended. The average disappearance of nasal discharge was five and one-half days and of membrane on the tonsils seven and one-third days, as opposed to the subcutaneous method which was two and two-third days.

With the injection of diphtheria antitoxin intravenously we have had no experience. E. Freedberger and S. Mita<sup>11</sup> claim from their experiments that larger doses may be borne and that there is less chance of an anaphylactic reaction when applied directly to the blood stream and so avoiding a reaction with the body tissues. In very desperate cases it might appeal to us as offering a better chance to more promptly neutralize the toxins.

Acetone was found in our diphtheria patients in only 28.5 per cent., but only one examination was made for each of the cases. F. Reicher,<sup>12</sup> of Hamburg, found it in 65 per cent. of his diphtheria patients during the febrile stage and in 40.2 per cent. of all other anginas and is, therefore, inclined to regard it as of diagnostic significance. I cannot see that it is needed especially as an aid,

<sup>9</sup> Münch. med. Woch. 1912, lix, 84.

<sup>11</sup> Deutsch. med. Woch., February, 1912.

<sup>10</sup> Deutsch. Arch. f. klin. Med., 1911.

<sup>12</sup> Münch. med. Woch., October, 1911.

for either a laboratory or clinical case of diphtheria will have its appropriate treatment. Even in private practice one should not be satisfied with just one negative culture.

Our routine method of staining for the Kelbs-Loeffler bacillus has been done with the standard Loeffler's methylene blue. Very recently we have tried in conjunction with this a stain proposed by Dr. Marie Raskin<sup>13</sup> in a paper read before the Royal Clinical Institute, of St. Petersburg. The solution is composed as follows: 5 c.c. of glacial acetic acid, 95 c.c. of distilled water, 100 c.c. of 95 per cent. alcohol, 4 c.c. of an old and long-standing methylene blue solution, 4 c.c. of Ziehl's carbol fuschin.

The method is to drop the mixture on the prepared slide and then boil over a flame for eight to ten seconds. After five seconds the slide is washed in water, dried, and examined. The polar bodies appear as deep blue, while the rod is a bright red.

Practically, our stains so far show the rods to be a pinkish color, while the granules stand out very well as dark bodies. Other rods and cocci likewise take the pink stain. From our limited experience in its use, it appears to be a good stain and I think that the polar bodies stand out more prominently than with the methylene blue method alone.

Before closing let me mention a few observations concerning measles and rubella. Our average white count for all ages in both was between 7000 and 8000, somewhat higher than we would expect. All had an increased polymorphonuclear count.

The cervical and submaxillary glands were enlarged in practically all of our rubella cases, but in none markedly so. The submental gland was enlarged in a few cases (recent cases show their presence more often), the post-auricular were enlarged more frequently. In rubella the rash was of the maculo-papular type in 81 per cent.; of the erythematous type in 19 per cent.

In measles, acetone and diacetic acid (each) were present in 22 per cent. which is, I believe, lower than usual. Indican occurred in 88 per cent.

In rubella both acetone and diacetic acid were negative in all cases, a fact which may be found to have some diagnostic significance; indican was positive in 50 per cent.

In conclusion I wish to express my appreciation of the efficient work done in the laboratory by Dr. William H. Peters, the bacteriologist, and by Mr. King and Mr. Bader, of the Ohio-Miami Medical School, whose results are incorporated in this article. To Dr. Samuel Zielonka I am indebted for several valuable translations. It would also be unfair to close without grateful recognition of the services of the internes and nurses who, from time to time, have been on duty at the hospital, for without their help this paper would have been impossible.

<sup>13</sup> Deutsch. med. Woch., December, 1911.

**STUDIES ON THE MOTOR FUNCTIONS OF THE STOMACH BY  
THE USE OF THE GASTRIC AND DUODENAL FISTULAS,  
ESPECIALLY AS REGARDS THE INFLUENCE OF THE  
BITTER WATERS AND BITTER SALTS, THAT IS,  
THOSE CONTAINING MAGNESIUM SULPHATE  
OR SODIUM SULPHATE.**

By THOMAS R. BROWN, M.D.,

ASSOCIATE IN MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

(From the Experimental Biological Division of the Pathological Institute of the University of Berlin.)

THE object of the experiments described in this article was to study the effect of various substances, especially salts and waters containing either magnesium sulphate ( $\text{MgSO}_4$ ) or sodium sulphate ( $\text{Na}_2\text{SO}_4$ ), the so-called bitter salts and bitter waters, upon the motor functions of the stomach. This was done by means of the low gastric fistula in one dog and the high duodenal fistula in three other dogs, determining in the former the quantity of residual fluid after a certain length of time, and in the latter the time required for all the fluid to pass, using the two methods synchronously for the study of the liquids in question. The dogs used were strong, healthy, and of moderate size, and had been kept fasting from eighteen to thirty hours before each experiment; the fluid to be tested was introduced by means of the ordinary stomach tube and funnel. If, as occurred several times during these experiments, especially after the use of highly concentrated solutions of the salts, the dog developed symptoms of an acute gastric catarrh, vomiting, anorexia, and the presence of considerable mucus occasionally slightly blood-streaked in the gastric contents, that dog was not used again until all signs and symptoms of the catarrh had entirely disappeared. The experiments were always comparative, that is, the solution to be tested was always compared as to its effect with an equal quantity of some other fluid, sometimes ordinary water, at other times some other solution of the same or of another salt, these experiments following each other after an interval of from one-half an hour to an hour or more, but always on the same day as the motor functions of the healthy stomach vary so markedly under different conditions, and are so much affected by surrounding circumstances, the amount of noise, the presence of unusual sights and sounds, psychic state of the animal, etc., that otherwise the results obtained would be of far less value. The liquids were all given at room temperature ( $18^\circ \text{C}$ ).

In the case of the gastric fistula the stomach was first drained thoroughly by removing the cork which stopped the opening, and then, after its return, 150 c.c. of fluid was administered, and the

residue withdrawn by removal of the cork in ten minutes (unless otherwise noted in our tables) and carefully measured. In the case of the duodenal fistula the cork was withdrawn and the upper duodenum drained, the cork replaced and 150 c.c. of the liquid given, a few drops of methylene blue or methyl-violet solution being used as an indicator (indigo-carmin powder in the case of the oils). The old method of withdrawing from 0.5 to 1 c.c. of fluid every two minutes was discarded as being far too unphysiological, as unquestionably the emptying of the stomach is dependent not only upon the reaction of the fluid in the duodenum, but also upon its quantity, and the withdrawal of the amount demanded by the older method changes markedly the pressure conditions in the duodenum, and results in the conclusion that the stomach empties itself more rapidly than under more physiological conditions. Our method was to withdraw about 1 c.c. of fluid every ten minutes for the first hour or even longer, then, as the change in the color suggested that the experiment was drawing to its close, every five minutes and finally every two minutes.

In a certain number of our experiments, quantitative determinations of the salt used and of the hydrochloric acid were made in the case of the gastric fistula and of the former alone in the case of the duodenal fistula, and then from our knowledge of the amount of the salt (usually sulphate) in the solution used and on the assumption that the acidity of the pure gastric juice of the healthy dog is practically constant (0.5 per cent.), we have attempted to determine the amount of gastric juice and transudate resulting from the use of the fluid in question in the gastric fistula, and the sum of gastric, duodenal, pancreatic, and biliary secretions, and transudate (or exudate) in the duodenal fistula. We have assumed for this that the amount of absorption of salts and water is *nil*, which is probably practically true in the case of the ten-minute experiment with the gastric fistula, but hardly approximately true with the duodenal fistula, as the time for the substances to be in contact with the mucous membrane is much longer, and the chances of absorption correspondingly greater. Nevertheless, we give the figures for what they may be worth, and in this connection we must not forget the poor powers of absorption of the magnesium salts and of sodium sulphate as many investigations have shown. In our quantitative determinations with the duodenal fistula, we have attempted to obtain the average salt content by taking 1 c.c. of the fluid withdrawn at ten-minute intervals, 0.5 c.c. at five-minute, and 0.2 c.c. at two-minute intervals, making our analysis from the mixed fluid so obtained.

In practically all our experiments, we determined the freezing points of the solutions used in order to determine whether we were dealing with iso-, hypo-, or hypertonic fluids. In a number of cases, notably with Hunyadi and Friedrichshall waters, by adding

enough water to make these fluids practically isotonic, we could obtain comparative results as to the influence of these well-known waters as usually administered, and when diluted to isotonicity, while with the various salts employed by us we could compare the effects of hypo-, iso-, and hypertonic solutions of the same salt by using solutions of different strength. It should be mentioned that the freezing point ( $\Delta$ ) of the dog's serum equals  $-0.6^{\circ}\text{C}$ . and not  $-0.56^{\circ}\text{C}$ ., as in the human being.

As to whether more exact data as regards the motor function of the stomach are to be obtained by the use of the gastric or duodenal fistula, each has its value. By the former we get a better idea of the amount of gastric secretion and transudate called forth; by the latter, especially if our more physiological method is employed, truer knowledge as to the exact time required by the solution to entirely leave the stomach.

Before giving the results of our experiments, the exact figures of which will be found in tabulated form at the end of this article, it may be of interest to briefly review some of the important literature as regards the motor functions of the stomach, especially, of course, the results obtained by the use of the x-rays in man and in animals, and of the gastric and duodenal fistulas in animals, and to a less extent, by the examination of the feces and by auscultation and palpation. The discovery of a definite anatomical separation between the fundus and the antrum pylori calls attention anew to the fact that the latter's function is distinct, the more thorough mixing of the liquid or semiliquid food (furnished by the fundus) with gastric juice and ejection into the duodenum. The so-called pyloric reflex determines to a great extent the length of time the food remains in the stomach, the stimulant being mechanical, according to Morris and von Mering, chemical according to the Pawlow school, both playing a part, according to Tobler, and this last seems the most probable. According to many observers, the true peristaltic waves arise practically only in the pyloric portion, although, according to Boldyreff, even in the fasting stomach rhythmic contractions appear at intervals of from one and one-half to two hours.

As to the length of time various fluids remain in the stomach, Cohnheim and Best,<sup>1</sup> found that physiological sodium chloride solution leaves the stomach quickest, water remains longer, and a 2 per cent. sodium chloride solution still longer. They found that the temperature of the fluid did not affect the motility, while Roeder<sup>2</sup> found that temperatures above or below  $37^{\circ}\text{C}$ . stimulate the motility.

According to Cohnheim<sup>3</sup> and Cannon<sup>4</sup> there are autonomous

<sup>1</sup> Zeit. f. physiol. Chemie, 1910, lxi, 117.

<sup>2</sup> Zeit. f. physiol. Chemie, 1910, lxi, 102.

<sup>3</sup> Amer. Jour. Physiol., 1906. xvii.

<sup>4</sup> Med. Klin., 1909, v, 816.



motor centres in the stomach, while the effect of psychic influences upon motility has been especially shown by the former. Perhaps our greatest knowledge of the motor functions of the stomach has come from the use of the x-rays in this field, inaugurated by Cannon and by Roux and Balthazar in 1897, and since then employed by many investigators in this connection. An interesting review of the work done along these lines is to be found in an article by Hertz,<sup>5</sup> which includes a number of important personal observations. According to Leven and Barret, 200 c.c. of water leaves the stomach, if already empty, in about twenty minutes, figures closely harmonizing with certain of our experiments on the dog with the gastric fistula, and which suggests that the pyloric sphincter does not become strongly contracted until after the ingestion of food. According to Carnot, Chessevant, and Otto, distilled water and anisotonic salt solutions generally remain longer in the stomach than isotonic solutions, probably due to the inhibition of the pyloric relaxation, and, to quote Hertz's discussion of these researches: "Consequently the chyme when it reaches the duodenum is much more nearly isotonic with the tissue fluids than when it reaches the stomach. The change is brought about in part by the secretion of fluid rich in salt in the case of hypotonic solution and distilled water, and by the secretion of ordinary gastric juice in the case of hypertonic solutions. Osmosis and diffusion undoubtedly help in both cases. The change is much less rapid in hypertonic than in hypotonic solutions, but even very concentrated solutions become almost isotonic before their evacuation from the stomach is complete." These conclusions do not agree with our findings, and the question of the effect of the osmotic pressure of a solution upon the gastric motility is still far from settled. It will be remembered in this connection that the absorptive power of the stomach is very slight in the case of most substances, practically *nil* with water. Although, as a rule, diffusion is determined by the osmotic pressure, Roth and Strauss, and Pfeiffer and Sommer have shown that in the case of the stomach unlike the serous cavities, this law does not hold good, for in this viscus the tendency is toward an osmotic pressure lower than that of the blood serum ( $\Delta = -0.56^{\circ}$  C. in human being,  $-0.6^{\circ}$  C. in dogs). According to Strauss this lower level corresponds to a freezing point of from  $-0.32^{\circ}$  C. to  $-0.48^{\circ}$  C. He therefore calls fluids with a freezing point less than  $-0.48^{\circ}$  C. gastrohypertonic, if above this figure gastrophypotonic. According to this investigator the free hydrochloric acid is only secreted when the stomach contents have reached this point; before this the fluid from the stomach wall is neutral or faintly alkaline. According to Roth and Strauss the reason for these phenomena is that the freezing point of the gastric juice equals  $-0.48^{\circ}$  C.; with

hypertonic solutions there is a streaming of water from the blood stream, and probably also a migration of more fixed molecules from stomach contents into plasma than in the reverse direction, while even with isotonic liquids this takes place until a degree of tonicity equal to that of the gastric juice is reached. With hypotonic solutions there is a difference of opinion, v. Mering, Moritz, and others holding that the flow of water from gastric contents into the blood stream is very slight, a view certainly borne out by our experiments, although Pfeiffer and Sommer believe that even here the law of osmotic pressure is followed. Rodari thinks these discrepancies can be explained by variations in osmotic pressure of the gastric juice, "but due to the slight permeability of the gastric mucous membrane to water, the water movement due to differences in osmotic pressure between the stomach contents and blood plasma takes place slowly so that another factor plays a part, and an important one, namely, the osmotic pressure of the stomach juice, which as it were, lies between the two and is capable of great variations, although usually hypotonic." According to the experiments of H. Strauss,<sup>6</sup> "a certain law seems to exist so that hypertonic solutions in the stomach are brought by dilution to a condition of lower osmotic pressure and remain longer in the stomach than hypotonic solutions," and this exactly harmonizes with our findings.

It is very difficult to explain all the facts regarding absorption from and transudation into the stomach on purely physical grounds, especially when we remember that most investigators hold that the gastric juice is of constant not varying composition, although, of course, as studied *extra vitam* by the usual methods, it may show wide variations, due to its degree of admixture with mucus, transudate, and ingesta.

As to the special effect of certain purgatives and laxatives, especially the bitter waters and bitter salts, upon the secretory and motor functions of intestines and stomach, much more work naturally has been done upon the intestinal side. Liebig believed that the action of salts was due to endosmosis, and therefore the greater the concentration of the salt the greater its purgative effect. Aubert, on the other hand, suggested that this was due more to chemical than to physical influences, that the quantity, not the concentration of the salt, was the important factor, and that the purgative action was due to the stimulation of the intestinal nerve-endings by the salt absorbed in the blood. Bauer, Moreau, and Brunton, from experiments with isolated intestinal loops, reached conclusions similar to those of Liebig; Hay suggested that the fluid poured out so abundantly was an exudate, not a transudate: while Hamburger combined the various theories, and suggested

<sup>6</sup> Physiol. Mineral-Stoffwechsel, Berlin, 1906.

that the purgative effect of the bitter salts depends on the increase of fluid in the intestinal canal due to gastric, intestinal, and possibly pancreatic secretion, to lessened absorption and increased peristalsis. Bickel<sup>7</sup> has shown that sodium sulphate and Hunyadi water distinctly inhibit the pancreatic secretion, and that the latter produces a diminution of the gastric secretion, especially of the hydrochloric acid; this was shown by him in the blind Pawlow stomach. According to Heinheimer, sodium and magnesium sulphate inhibit the secretion of hydrochloric acid, while Sasaki found that Carlsbad water occupies a middle position between the excitosecretory and the depressosecretory waters, agreeing with the clinical findings of Jaworski that small repeated doses of Carlsbad water increase the gastric secretion, large doses, if continued, inhibit its secretion more and more. Tausoni and Morfiori believe that the purgative action of the bitter waters is due to the great increase of mucus which hinders absorption, while to lessened absorption F. Frankl also ascribes this action, as he found no increase of peristalsis nor a transudation into the intestine after the injection of sodium sulphate into the blood. J. B. MacCallum, however, found both increased peristalsis and increased passage of fluid from intestinal wall into intestine after the intravenous administration of the bitter salts; according to Headland, Mendel, and others, this same effect is produced when the salts are given by mouth by their absorption in the upper intestine and secretion later into the lower intestine together with a large amount of transudate. Hertz<sup>8</sup> from *x*-ray studies reached conclusions similar to those of Aubert and MacCallum, namely, that saline purgatives cause little or no acceleration in the passage of the chyme through the small intestine, but that the colon is markedly affected, and that "some of the purgative salt must have been absorbed from the stomach or small intestine into the blood from which it acted directly upon the neuromuscular mechanism, producing motor and secretory activity in the way described by MacCallum." Ury,<sup>9</sup> in a most exhaustive series of analyses of the salts and ferments of the feces, after the administration of various purgatives to men and to animals, concluded that the bitter salts in large doses act by causing a local irritation of the nerve plexus lying in the intestinal wall, increasing peristalsis, and calling forth a strong transudation of a watery fluid. The marked increase of peristalsis is not explained by the increase of the fluid, but is primary in nature, and coördinate with the transudation. Mucus was absent, or present in very small amount, and there was a moderate increase of the intestinal juice. In small doses as used in practice for laxative purposes, increased peristalsis and transudation were present, but to a lesser

<sup>7</sup> Berl. klin. Woch., 1906, No. II.

<sup>8</sup> Guy's Hospital Reports, 1909, lxiii.

<sup>9</sup> Arch. f. Verdauungskrankh., 1909, xv, 210, and Biochem Zeitschr., 1910, xxiii, 153.

extent, and here comes into play the poor power of absorption of the magnesium salts, and the retention of their water of solution, and isotony of the fluid contents of the small intestines is not reached. As to the effect of other laxatives, Ury found after senna an increase of fluids, hypersecretion of pancreatic juice, a colossal increase of diastase, absence of pepsin and lipase, and an increase in the secretion of the small intestine, as shown by the presence of maltase, invertin and a trace of nuclease, while, on the other hand, Ascher and Spiro found that senna, rhubarb, cascara, and aloes act only through increased peristalsis, and Brieger, in dogs, and Flemming, in rabbits, found no increase in the intestinal secretion and no reddening of the mucosa in isolated loops of intestine. Magnus<sup>10</sup> found that castor oil produced increased peristalsis in both small and large intestines, senna only in the large intestine; thus, as regards peristalsis, the former acts like large doses of magnesium sulphate, the latter like small doses, according to Ury.

The results of our experiments were as follows:

A. WITH HUNYADI JANOS AND FRIEDRICHSHALL WATERS. The detailed results of these as of all our other experiments will be found in tabulated form at the end of this article, and we shall here simply call attention to certain points of interest, especially the influence of the tonicity of the fluid, and the results of quantitative studies of the amount of gastric juice secreted, and the extent of the transudation. The freezing point of Hunyadi water is  $-1.03^{\circ}\text{C.}$ , of Friedrichshall  $-1.15^{\circ}$ , of tap water  $-0.03^{\circ}\text{C.}$ , and dog serum  $-0.6^{\circ}\text{C.}$ , that is, each of these waters is strongly hypertonic, while a dilution of each with an equal amount of tap water will give almost isotonic solution ( $\Delta$  of 50 per cent. Hunyadi =  $-0.51^{\circ}\text{C.}$ , of 50 per cent. Friedrichshall =  $-0.6^{\circ}\text{C.}$ ).

A consideration of the figures in the tables will show that the motor functions of the stomach tested both by the gastric and the duodenal fistula methods are very strongly inhibited by these hypertonic waters, while if diluted about to isotonicity, the difference between their action and that of tap water as regards gastric motility is very slight. This and in fact all our experiments have shown that it is impossible to explain the absorption and motor phenomena of the stomach on purely physical grounds alone, as otherwise the almost isotonic 50 per cent. Hunyadi and Friedrichshall solutions would leave far more rapidly than the strongly hypotonic tap water; in reality the latter leaves the organ a little sooner.

The question of the amount of gastric juice and transudate called forth by these waters was considered quantitatively. In Friedrichshall water in 10 c.c. the amount of sulphates calculated as barium sulphate ( $\text{BaSo}_4$ ) equals 0.2292 gram, in Hunyadi water

0.598 gram.; the acidity of the pure gastric juice of the dog is assumed to be 0.5 per cent.

In Experiments 6, 7, and 8 of our series with the gastric fistula the following figures were obtained; the first two were experiments of ten minutes, the last of twenty minutes; 150 c.c. of fluid was given in each case.

#### EXPERIMENT 6.

Solution used.	Amount of fluid obtained.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates in 10 c.c. as Ba SO <sub>4</sub> .	Gastric juice.	Transudate.
Tap water . . . .	46 c.c.	6	0.0	2.0 c.c.	
50 per cent. Hunyadi . .	77 c.c.	4	0.2388 gram	2.5 c.c.	13.0 c.c.
Hunyadi . . . .	104 c.c.	4	0.4948 gram	3.7 c.c.	15.3 c.c.

#### EXPERIMENT 7.

Tap water . . . .	79 c.c.	6	0.0	3.5 c.c.	
50% Friedrichshall . .	76 c.c.	6	0.0972 gram	3.3 c.c.	8.3 c.c.
Friedrichshall . . . .	121 c.c.	4	0.1928 gram	3.3 c.c.	16.6 c.c.

#### EXPERIMENT 8.

Tap water . . . .	18 c.c.	60	0.0	7.9 c.c.	
50% Friedrichshall . .	30 c.c.	55	0.0546 gram	12.0 c.c.	2.7 c.c.
Friedrichshall . . . .	74 c.c.	23	0.1289 gram	12.4 c.c.	19.1 c.c.

These experiments show, in the first place, that in ten minutes very little gastric juice is secreted, while in twenty minutes the percentage is much higher. In the second place, a considerable transudation is present with both solutions, more with the hypertonic than with the isotonic fluids, but transudate and gastric juice combined were not enough to account for the amount of liquid remaining in the stomach in the case of the pure Hunyadi and Friedrichshall waters, and, therefore, these waters besides calling forth considerable transudation and some secretion of gastric juice, undoubtedly also strongly inhibit the motor functions of the stomach. Number 4 of our series of experiments with the gastric fistula was very instructive in that it showed that this inhibitory effect disappears quickly after the hypertonic solution has left the stomach; with oil, however, which does not leave the stomach completely, but coats the mucous membrane with a covering difficult to remove, this inhibiting influence persists much longer, as seen in Experiment 5.

It must not be forgotten, however, that all these results are based on the assumption that during the short time of the experiment practically no absorption of salts or water by the stomach takes place. Occasionally in the case of these waters and also with strongly hypertonic solutions of Carlsbad salts and magnesium sulphate, in some instances a true, acute gastric catarrh, with all the characteristic signs and symptoms, was produced, necessitating the discontinuance of the experiments until the stomach was completely cured.

In the case of the duodenal fistula, in Experiment 6, a quantitative sulphate determination was made with the following results:

Solution used (150 c.c.).	Time to pass duodenal fistula.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates in 10 c.c. as BaSO <sub>4</sub> .
Hunyadi . . . . .	2 hours 10 minutes	8	0.1374 gram
50% Hunyadi . . . . .	1 hour 25 minutes	7	0.112 gram

This would mean, assuming that there has been practically no absorption of salts or water, that after the giving of 150 c.c. pure Hunyadi water, the sum of the biliary, gastric, duodenal, pancreatic, and mucous secretions and of transudate called forth equalled 503 c.c., while after 150 c.c. of almost isotonic 50 per cent. Hunyadi, only 250 c.c. was called forth. Another experiment in this connection may be of interest: To one of the duodenal fistula dogs was given 130 c.c. pure Hunyadi water and all the fluid from the duodenal fistula collected. Although, of course, the major portion must have passed by the fistulous opening along the much broader upper intestine, nevertheless, in one and one-half hours 182 c.c. was obtained from the fistula.

B. WITH CARLSBAD SALTS. We made a few experiments with natural and artificial Carlsbad salts (the latter, as a rule, being 44 parts Na<sub>2</sub>SO<sub>4</sub>, 36 parts NaHCO<sub>3</sub>, 18 parts NaCl, and 2 parts K<sub>2</sub>SO<sub>4</sub>). Of the waters obtained at the springs, Sprudel has a freezing point of  $-0.307^{\circ}$  C., Muhlbrunnen  $-0.293^{\circ}$  C., Franz Joseph  $-0.290^{\circ}$  C.; of solutions of the natural salts, in 1 per cent. solutions  $\Delta = -0.47^{\circ}$  C., in 5 per cent.  $\Delta = -1.88^{\circ}$  C.; while of the artificial salts in 2 per cent. solution  $\Delta = -0.3^{\circ}$  C., in 5 per cent.  $\Delta = -0.77^{\circ}$  C., that is, of the artificial salts a 3 per cent. solution is about isotonic, a 10 per cent. solution strongly hypertonic. A considerable inhibition of gastric motility is seen with hypertonic solutions with both methods, while, as with Hunyadi and Friedrichshall water, even with isotonic solutions some transudation is called forth, and the solutions take a slightly—although only very slightly—longer time to entirely leave the stomach than ordinary tap water. The secretion of gastric juice after Carlsbad solutions is certainly no more, and probably slightly less than after ordinary water.

One quantitative experiment (Number 3) was made with the gastric fistula as follows:

#### EXPERIMENT 1.

Solution used (150 c.c.).	Amount obtained in ten minutes.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates in 10 c.c. as BaSO <sub>4</sub> .	Amount of gastric juice.	Amount of transudate.
Tap water . . . . .	12 c.c.	60	0.0	5.2 c.c.	
3% solution of artificial salt . . . . .	22 c.c.	20	0.2605 gram	3.2 c.c.	8.5 c.c.
10% solution of artificial salt . . . . .	88 c.c.	10	0.7277 gram	6.4 c.c.	47.2 c.c.

This experiment again calls attention to the enormous amount of transudate called forth by strongly hypertonic solutions, and also to their marked inhibitory effects upon gastric motility. These strong solutions of Carlsbad salt frequently showed their markedly irritating effect upon the mucous membrane by producing the typical symptoms of an acute gastritis, the secretion of mucus in large amount, sometimes blood-stained, anorexia, vomiting, etc.

C. WITH MAGNESIUM SULPHATE (EPSOM SALT— $\text{MgSO}_4$ ). Of solutions of magnesium sulphate in solutions of 1 per cent.  $\Delta = -0.13^\circ \text{C.}$ , of 3 per cent.  $\Delta = -0.32^\circ \text{C.}$ , of 10 per cent.  $\Delta = -0.71^\circ \text{C.}$ , and 20 per cent.  $\Delta = -1.45^\circ \text{C.}$ , and a 7.5 per cent. solution is practically isotonic. These figures were obtained with solutions of the ordinary Epsom salt bought at the drug store. In 10 c.c. of a 20 per cent. solution, the amount of sulphates calculated as  $\text{BaSO}_4 = 1.8937$  grams.

With the weak solutions of this salt we had a good opportunity to study the effect of strongly hypotonic solutions. With the duodenal fistula, the 1 per cent. solution and water seemed to take practically the same time, the 3 per cent. solution distinctly longer—an interesting fact when we remember that the latter contains more of the salt in solution and is closer to isotonicity.

Two quantitative experiments with the gastric fistula (Numbers 2 and 3) were made with the following results:

#### EXPERIMENT 2.

Solution used (150 c.c.).	Amount obtained in ten minutes.	Acidity in $\frac{N}{10}$ NaOH.	Sulphates of 10 c.c. as $\text{BaSO}_4$ .	Amount in gastric juice.	Amount of transudate.
Water . . .	24 c.c.	8	...	1.4 c.c.	
1% $\text{MgSO}_4$ . .	36 c.c.	30	...	7.9 c.c.	
3% $\text{MgSO}_4$ . .	58 c.c.	12	...	5.1 c.c.	

#### EXPERIMENT 3.

Water . . .	29 c.c.	13	0.0	2.5 c.c.	
7.5% $\text{MgSO}_4$ .	38 c.c.	12	0.4512 gram	3.3 c.c.	10.6 c.c.
20% $\text{MgSO}_4$ .	98 c.c.	8	1.2296 gram	6.0 c.c.	28.5 c.c.

These figures again show the marked inhibition of gastric motility and the stimulating effect upon transudation of strongly hypertonic solutions; and also that the difference between the effects of water, isotonic and hypotonic solutions upon gastric motility is but slight—the salt solutions retarding it a little, possibly due to the transudate they undoubtedly call forth, while as regards the amount of gastric juice secreted, some solutions seem to call forth more than water, others less.

D. WITH SODIUM SULPHATE (GLAUBER'S SALT— $\text{Na}_2\text{SO}_4$ ). The 1 per cent. solution of this salt has a freezing point of  $-0.36^\circ \text{C.}$ , the 3 per cent. solution of  $-0.82^\circ \text{C.}$  The results obtained harmonized with those previously described as regards the influence of hypertonic and hypotonic solutions.

E. WITH OLIVE AND CASTOR OILS. These experiments simply called attention to the already well known fact that oils markedly inhibit the motor functions of the stomach; of the two castor oil retarded the gastric movements most, and this was probably due to its greater irritating effect, as, with this as with the other substances tested, the stomach seems to act in a manner just opposite to the intestine, that is, the more the mucous membrane of the former viscus is irritated, the more its motor function is inhibited.

F. WITH OTHER SUBSTANCES. We have added a few experiments made with various other substances which may be of some interest. Strong tea seemed to inhibit the gastric motility, and also mesothorium emanations, although to a less extent.

Two experiments were made with the gastric fistula with the well-known Roumanian diuretic water, Caciuglata, of which the freezing point is  $-0.17^{\circ}$  C.; that is, it is strongly hypotonic. It and tap water left the stomach in practically the same time, and in this, as in many other cases, we have repeated the experiment in the reverse direction, that is, if we gave water first and then the fluid to be tested in the first experiment, this order was reversed in the second; by this means our results should be more accurate, for if the animal is more fatigued at the time of administration of the second dose, and thereby perhaps the motor function slightly inhibited, this will be discounted by the results obtained in the reversed experiment. With this water we performed two quantitative experiments, here comparing the phosphate-content (as magnesium phosphate) of the fluid obtained from the gastric fistula with that of the diuretic water itself, in 25 c.c. of which there is 0.0063 gram. The results of these experiments were as follows:

Solution used (150 c.c.).	Amount obtained in fifteen minutes.	Acidity in $\frac{N}{10}$ NaOH.	Phosphates in 25 c.c. as Mg- phosphate.	Amount of gastric juice.	Amount of transudate.
Water . . .	59 c.c.	29	0.0	12.5 c.c.	
Caciuglata water	44 c.c.	37	0.00325 gram	11.8 c.c.	9.6 c.c.
Caciuglata water	22 c.c.	30	...	4.8 c.c.	
Water . . .	18 c.c.	25	...	3.3 c.c.	

In a number of other experiments both with the gastric and the duodenal fistula, we could show the extremely marked inhibitory effect of various emotions, such as fatigue and of surrounding disturbances, such as noise, upon the motor function of the stomach. This, of course, accentuates the fact that an animal should never be used for experimental purposes until it has become habituated to standing for a considerable period of time without being fatigued, and also that it is essential that the experiments be carried out in a room as free as possible from noise, excitement, and unusual sights and sounds.

The main conclusions which we may draw from this series of experiments are as follows:



By the use of both the gastric and the duodenal fistula, and in the latter case we suggest our modification of the usual method as a much closer approximation of physiological conditions, we may obtain data of comparative exactness as to the influence of various substances upon the motor functions of the stomach. By the duodenal method we obtain figures of greater exactness as to the comparative times required by various liquids to entirely leave the stomach, by the gastric method we learn more about the effect of these liquids upon gastric secretion and transudation; we would suggest that the two methods always be employed simultaneously.

As to the influence of the various bitter waters and solutions of the bitter salts—all of which depend in the main for their action upon magnesium or sodium sulphate, strongly hypertonic solutions or waters markedly inhibit gastric motility, besides producing a great transudation into the stomach as well as a secretion of gastric juice, which latter may be more or less than that obtained after the administration of ordinary tap water. If these salts are given in very strong solution, their irritating effects are seen in certain instances by the appearance of the typical signs and symptoms of an acute gastritis.

By the use of quantitative analyses of the hydrochloric acid and sulphates in the fluid obtained from gastric or duodenal fistula, we may get some idea of the extent of the secretion and transudation.

Isotonic solutions leave the stomach much sooner than strongly hypertonic solutions, and do not call forth so much transudate as the latter, and much less frequently, although occasionally, produce irritating effects upon the gastric mucous membrane. This suggests the inadvisability of using hypertonic solutions of the bitter salts in gastric disorders with atony or with a diseased condition of the mucous membrane, even if thereby the desired laxative or purgative effect is diminished.

As a rule isotonic and hypotonic solutions leave the stomach a little less rapidly than the very hypotonic tap-water, possibly due to the transudate called forth by the former fluids, although this is of much less extent than after hypertonic solutions; the secretion of gastric juice may be slightly more or slightly less with these solutions than with ordinary water. This again calls attention to the fact that it is impossible to explain the motor and absorptive phenomena of the stomach on purely physical grounds, even when, in addition to the ordinary laws governing diffusion and osmosis, we assume the interposition between gastric cavity and gastric wall of a gastric juice of varying tonicity.

A comparison between the action of the bitter salts and bitter waters upon the motor functions of the stomach with those of the intestine, shows that their action is reversed, inhibitory in the former case, stimulating in the latter, while in both cases transudation is markedly stimulated.

The complete figures of all the experiments follow:

### MOTILITY EXPERIMENTS.

#### A. WITH HUNYADI JANOS (H) AND FRIEDRICHSHALL (F) WATERS.

##### *First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	22 c.c.
	H	150 c.c.	10 minutes	91 c.c.
	F	150 c.c.	10 minutes	71 c.c.
2	Water	150 c.c.	10 minutes	68 c.c.
	F	150 c.c.	10 minutes	122 c.c.
	H	150 c.c.	10 minutes	98 c.c.
3	Water	150 c.c.	10 minutes	44 c.c.
	H	150 c.c.	10 minutes	104 c.c.
4	Water	150 c.c.	10 minutes	28 c.c.
	Water with mesothorium	150 c.c.	10 minutes	38 c.c.
	F	150 c.c.	10 minutes	92 c.c.
	Water	150 c.c.	10 minutes	48 c.c.
	H	150 c.c.	10 minutes	107 c.c.
5	Water	100 c.c.	10 minutes	24 c.c.
	Olive oil	100 c.c.	10 minutes	84 c.c.
	H	100 c.c.	10 minutes	85 c.c.
	F	100 c.c.	10 minutes	104 c.c.
6	Water	150 c.c.	10 minutes	46 c.c.
	50 per cent. H	150 c.c.	10 minutes	77 c.c.
	H	150 c.c.	10 minutes	104 c.c.
7	Water	150 c.c.	10 minutes	79 c.c.
	50 per cent. F	150 c.c.	10 minutes	76 c.c.
	F	150 c.c.	10 minutes	121 c.c.
8	Water	150 c.c.	20 minutes	18 c.c.
	50 per cent. F	150 c.c.	20 minutes	30 c.c.
	F	150 c.c.	10 minutes	74 c.c.

##### *Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	H	150 c.c.	1 hour 36 minutes
	F	150 c.c.	1 hour 17 minutes
2	Water	150 c.c.	1 hour 18 minutes
	H	150 c.c.	2 hours 9 minutes
3	F	150 c.c.	2 hours 25 minutes
	Water	150 c.c.	1 hour 52 minutes
4	50 per cent. F	150 c.c.	1 hour 17 minutes
	F	150 c.c.	2 hours 19 minutes
5	H	150 c.c.	2 hours 10 minutes
	50 per cent. H	150 c.c.	1 hour 25 minutes

## B. WITH CARLSBAD SALT, NATURAL (N) AND ARTIFICIAL (A).

*First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	1 per cent. N	150 c.c.	10 minutes	68 c.c.
	5 per cent. N	150 c.c.	10 minutes	92 c.c.
	1 per cent. N	150 c.c.	20 minutes	3 c.c.
2	Water	150 c.c.	20 minutes	4 c.c.
	1 per cent. N	150 c.c.	20 minutes	8 c.c.
3	Water	150 c.c.	10 minutes	12 c.c.
	3 per cent. A	150 c.c.	10 minutes	22 c.c.
	10 per cent. A	150 c.c.	10 minutes	88 c.c.

*Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	Water	150 c.c.	55 minutes
	5 per cent. N	150 c.c.	1 hour 42 minutes
2	1 per cent. N	150 c.c.	1 hour 4 minutes
	5 per cent. N	150 c.c.	1 hour 28 minutes

## C. WITH EPSOM SALT.

*First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	3 per cent. E	150 c.c.	10 minutes	54 c.c.
	1 per cent. E	150 c.c.	10 minutes	60 c.c.
	Water	150 c.c.	10 minutes	69 c.c.
2	Water	150 c.c.	10 minutes	24 c.c.
	1 per cent. E	150 c.c.	10 minutes	36 c.c.
	3 per cent. E	150 c.c.	10 minutes	58 c.c.
3	Water	150 c.c.	10 minutes	29 c.c.
	7½ per cent. E	150 c.c.	10 minutes	38 c.c.
	20 per cent. E	150 c.c.	10 minutes	98 c.c.

*Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	1 per cent. E	150 c.c.	1 hour 1 minute
	3 per cent. E	150 c.c.	1 hour 42 minutes
2	3 per cent. E	150 c.c.	1 hour 58 minutes
	1 per cent. E	150 c.c.	1 hour 37 minutes
3	Water	150 c.c.	1 hour 34 minutes
	1 per cent. E	150 c.c.	1 hour 26 minutes

## D. WITH GLAUBER'S SALT (G).

*First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	41 c.c.
	1 per cent. G	150 c.c.	10 minutes	84 c.c.
	3 per cent. G	150 c.c.	10 minutes	98 c.c.

*Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	1 per cent. G	150 c.c.	1 hour 21 minutes
	3 per cent. G	150 c.c.	1 hour 35 minutes

## E. WITH OLIVE OIL AND CASTOR OIL.

*First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Olive oil, 30 c.c. }	150 c.c.	10 minutes	106 c.c.
	Water, 120 c.c. }			
	Castor oil, 30 c.c. }	150 c.c.	10 minutes	82 c.c.
	Water, 120 c.c. }			
2	Water	100 c.c.	10 minutes	24 c.c.
	Olive oil	100 c.c.	10 minutes	84 c.c.

*Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	Olive oil, 30 c.c. }	150 c.c.	1 hour 38 minutes
	Water, 120 c.c. }		
	Castor oil, 30 c.c. }	150 c.c.	2 hours 24 minutes
	Water, 120 c.c. }		
2	Olive oil	40 c.c.	2 hours 43 minutes
	Castor oil	40 c.c.	3 hours 40 minutes

## F. DIVERSE OBSERVATIONS.

*First Series, with Gastric Fistula.*

Experiment.	Substance.	Amount given.	Time.	Amount obtained.
1	Water	150 c.c.	10 minutes	54 c.c.
	Water c., 0.1 gram phenolphthalein	150 c.c.	10 minutes	76 c.c.
2	Water	150 c.c.	10 minutes	54 c.c.
	Strong tea	150 c.c.	10 minutes	80 c.c.
3	Water	150 c.c.	10 minutes	28 c.c.
	Water c., mesothorium (14,000 Mache-units)	150 c.c.	10 minutes	38 c.c.
4	Water	150 c.c.	15 minutes	59 c.c.
	Caciuglata water	150 c.c.	15 minutes	44 c.c.
5	Caciuglata water	150 c.c.	15 minutes	30 c.c.
	Water	150 c.c.	15 minutes	25 c.c.

*Second Series, with Duodenal Fistula.*

Experiment.	Substance.	Amount.	Time.
1	Water, 145 c.c. } Alcohol, 5 c.c. }	150 c.c.	1 hour 34 minutes
	Water, 145 c.c. } Alcohol, 5 c.c. } Phenolphtha- lein, 0.1 gram }	150 c.c.	1 hour 57 minutes
2	Water	150 c.c.	1 hour 34 minutes
	Strong tea	150 c.c.	2 hours 10 minutes
3	Water	150 c.c.	55 minutes
	Water c. mesothorium (8400 Mache-units)	150 c.c.	1 hour 36 minutes
4	Water	150 c.c.	1 hour 28 minutes
	Water c. mesothorium (14,000 Mache-units)	150 c.c.	2 hours 21 minutes
5	Fachingen water	150 c.c.	1 hour 28 minutes
	Selters water	150 c.c.	1 hour 4 minutes

## THE MORE COMMON FORMS OF CARDIAC IRREGULARITY, WITH THE REPORT OF A CASE OF HEART-BLOCK.<sup>1</sup>

By THOMAS A. CLAYTOR, M.D.,

CLINICAL PROFESSOR OF MEDICINE, GEORGE WASHINGTON UNIVERSITY; PHYSICIAN TO GARFIELD HOSPITAL AND TO THE TUBERCULOSIS HOSPITAL, WASHINGTON, D. C.

THIS subject has been taken up because I believe that it has been too much neglected by the rank and file of internists. I think that one might say without fear of contradiction that without some previous knowledge gained by the instrumental study of the pulse, either with the polygraph or the electrocardiograph, there are but few who are able to interpret, with any degree of accuracy, the various forms of irregular pulse and are, therefore, unable to give them their proper value as to prognosis and treatment.

That such knowledge may be at times of great importance I hope to show in the following pages.

In the last sixteen years, epoch-making discoveries have materially advanced our knowledge of the histological anatomy of the heart and of its rhythmic action. In fact, A. R. Cushny<sup>2</sup> said that although the study of the pulse had extended as far back as

<sup>1</sup> Read before the American Climatological Association, June 11, 1912.

<sup>2</sup> AMER. JOUR. MED. SCI., 1911, p. 1198.

medical history, more progress had been made, in certain directions, in the last fifteen years than in the previous century. As pioneers in the work upon cardiac arrhythmia, the names of Mackenzie, Wenckebach, and Hering probably stand out most prominently.

Putting aside any discussion as to the relative merits of the neurogenic or the myogenic origin of the heart beat, it is found most convenient to study cardiac arrhythmia, keeping always before us the qualities which have been assigned to the heart muscle, which are: (1) Stimulus production, the power to produce a stimulus which will excite the heart to contract; (2) excitability, the power to receive a stimulus; (3) conductivity, the power to convey a stimulus from one part of the heart to another; (4) contractility, the power to contract on being stimulated; (5) tonicity, the power to remain in a certain degree of contraction even when the active stimulation has ceased.

Under normal conditions the cardiac contraction begins in the specialized tissue at the junction of the descending cava and the right auricle, spreading thence to the rest of the heart. This, the sino-auricular node (Keith and Flack<sup>3</sup>), is then the pace-maker of the heart and the rhythmic contraction having its origin here is called the fundamental rhythm. In the wall of the right auricle near the coronary sinus is another specialized area, the auriculo-ventricular node (Tawara<sup>4</sup>), and it is from this point that arises the auriculoventricular bundle of Kent<sup>5</sup> and His, Jr.,<sup>6</sup> which forms the connecting link for impulses between the auricles and ventricles dividing into two limbs, the one passing to the right and the other to the left ventricle.

While there are instances of cardiac irregularity which are difficult to classify, the majority fall under the following heads: (1) Sinus or youthful arrhythmia; (2) premature contraction or extra systole; (3) heart-block (partial or complete); (4) the wholly irregular pulse (auricular fibrillation); with perhaps the addition of (5) the pulsus alternans, though the last named is an irregularity as to volume rather than as to time.

Some authors assign each of these forms of irregularity to a disorder of some one of the special qualities of the cardiac muscle. Thus sinus arrhythmia is said to be due to disturbance of the sino-auricular node in its impulse producing quality, the extra systole to disturbance of irregularity of the muscle; heart-block to disturbance of conductivity; auricular fibrillation to disturbance of contractility. If this be true, the whole study of cardiac arrhythmia is greatly simplified, but it has not yet been proved.

<sup>3</sup> Jour. Anat. and Physiol., 1907, xli, 172.

<sup>4</sup> Das Reizleitungssystem des Säugtierherzens, Jena, 1908.

<sup>5</sup> Jour. of Physiol., 1893, xiv, 233 to 254.

<sup>6</sup> Die Thätigkeit des embryonalen Herzens und deren Bedeutung für die Lehre von der Herzbewegung beim Erwachsenen, Arbeiten aus der Medizinischen Klinik, Leipzig, 1893, p. 14 to 49

I shall now briefly consider the most striking characteristics of the above named forms of arrhythmia as they are portrayed in polygraphic tracings, together with their etiology, pathology, diagnostic, and prognostic value.

As the appreciation of the abnormal polygraphic tracing is absolutely dependent upon an understanding of the normal, we may with profit refresh our memories by a brief consideration of Fig. 1. It may be seen that in the venous tracing there are three distinct upward (positive) waves (*a*, *c*, and *v*) and as many downward (negative) waves (*x*, *x'*, and *y*). The *a* wave in the venous tracing is produced by the state of increased pressure in the jugular vein resulting from the contraction of the right auricle; the *c* wave, while it is not wholly due to the carotid pulsation, for all clinical purposes may be considered to make its appearance synchronously with the beat of that vessel at the same level of the neck. The time between *a* and *c* is known as the *a-c* interval, and is of great importance, as it determines the state of conductivity between the

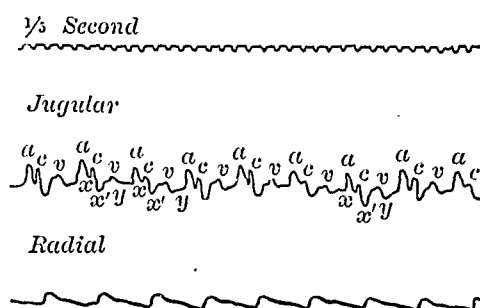


FIG. 1.—Polygraphic tracing of the normal.<sup>7</sup>

auricles and ventricles. The *v* wave, often called the ventricular wave, makes its appearance during ventricular systole, reaching its highest point just before the auriculoventricular valves open. The negative waves *x* and *x'* (usually considered as one), are probably the result of three factors: the relaxation of the auricular walls in early diastole; the state of negative intrathoracic pressure consequent upon the ventricular systole; and the dragging down of the auriculoventricular septum during ventricular contraction. The *y* wave occurs as the result of a state of negative pressure in the ventricles during their diastole, at the same time the auriculoventricular valves open and allow the blood to pass into the ventricles.

The arterial tracing (usually the radial) is necessary for the identification of the important elements of the venous curve.

<sup>7</sup> Through a misunderstanding the identification markings were not reproduced in the figures, but as the writing pens were of equal length the fixation points may be taken from the right border of the tracings.

Thus the *c* wave may be determined by the fact that it appears one-tenth of a second before the radial impulse, the *a* wave because it appears one-fifth of a second before the *c* wave, and the *v* wave by the fact that its apex occupies the same relative position in the venous tracing as does the dicrotic notch in the radial. As pointed out by Lewis,<sup>8</sup> the proper identification of the *v* wave may be of considerable importance in the correct reading of a tracing in which heart-block is suspected.

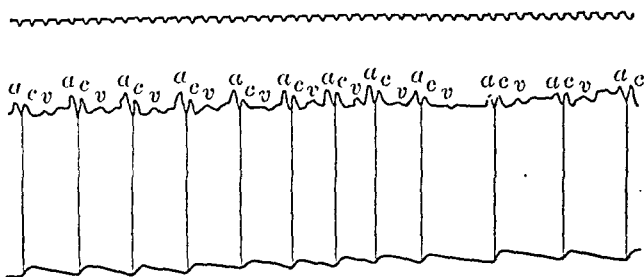


FIG. 2.—Sinus or youthful arrhythmia.

SINUS, OR YOUTHFUL ARRHYTHMIA, may best be described as a difference in the time rate of the cardiac contractions with but little difference, if any, in their force. When venous and arterial tracings are taken simultaneously it will be noted that they are perfectly synchronous in their corresponding details. The arterial tracing will show the systolic peaks to be of about the same height but at varying distances from each other. The irregularity is best seen in a slow pulse, since rapidity, by reducing the diastolic pause, has a tendency to lessen the abnormality. A similar form of arrhythmia may be produced in normal individuals by causing them to take some forced inspiration. The pulse will be found to become more rapid during inspiration and slower during expiration. The cause of sinus irregularity is reflex, coming through the vagi, and does not have its origin in the heart itself. It is observed in young and nervous individuals, also during convalescence from illnesses such as epidemic influenza, etc. It may or may not be noted by the patient, often it is not, though occasionally the diastolic pause is so prolonged as to produce cerebral anemia with syncope. The prognosis is good in all cases. It may be relieved by atropia.

EXTRASYSTOLE. According to Mackenzie,<sup>9</sup> the term "extrasystole" should be limited to those premature contractions of auricle or ventricle in response to a stimulus from some abnormal point of the heart, but where otherwise the fundamental or sinus rhythm of the heart is maintained.

<sup>8</sup> British Med. Jour., 1911, i, 593.

<sup>9</sup> Diseases of the Heart, 1903, p. 142.



Clinically there are recognized three varieties of extrasystole: the auricular, the ventricular, and the auriculoventricular, depending upon the point from which the abnormal stimulus takes its origin. Before going further it may be well to call attention to some physiological facts. It has been shown that if the ventricle be stimulated at any time during diastole (the receptive period of the cycle) it will respond by contracting, but that the force of the contraction is entirely independent of the strength of the stimulation. In other words, the ventricle responds with its entire strength to any stimulus which is sufficient to cause a contraction; the "all or nothing" phenomenon of Bowditch. During systole the ventricle is in the so-called refractory period of the cycle, when it will fail to respond to any stimulation. The strength of the ventricular contraction depends on the amount of energy which there has been time to accumulate. If then the stimulation has been premature the contraction will be feeble, if delayed, correspondingly strong.

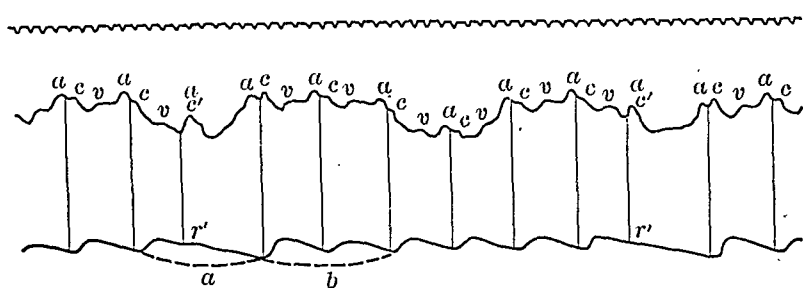


FIG. 3.—Showing extraventricular systoles,  $r'$  and  $r'$ , the one toward the right being too weak to appear in the radial tracing.

In Fig. 3 we have an example of ventricular extrasystole. In the radial tracing at  $r'$  may be seen the evidence of a premature and weak pulse beat. In the venous tracing the peak marked  $c'$  represents the premature ventricular contraction. It corresponds in general outline fairly well with the  $c$  peaks, but is earlier in the cycle and is quite a little higher; in this instance the ventricular contraction has occurred at the same time as the auricular, thereby throwing the  $a$  wave and the  $c$  wave together, which accounts for its unusual height. This auricular contraction is not followed by the usual ventricular contraction because the ventricle was in systole (the refractory stage) at the time the auricular impulse reached it. This accounts for the longer pause after  $r'$ , which is known as the compensatory pause. If a measurement be made it will be found that the space between the radial pulsation immediately preceding  $r'$ , plus that immediately following it, is the same as the distance occupied by two whole cycles of the regular beating ventricles. In other words ( $a = b$ ). It may also be determined by measurement that the auricular rhythm is not disturbed,

that is, the *a* waves occur at practically regular intervals from each other in spite of the disturbed ventricular rhythm as shown by the extrasystole. In some instances the *c* wave actually precedes the *a* wave in the venous tracing. Occasionally in a slowly beating heart the ventricle has had time to recover sufficiently after an extrasystole to respond to the auricular impulse as it would if there had been no extraventricular beat, and we have then an interpolated ventricular contraction. The impulse for a ventricular extrasystole has its origin in that portion of the bundle of His beyond the node of Tawara or in its ramifications in the ventricle.

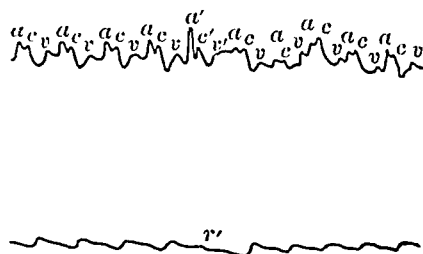


FIG. 4.—Auricular extrasystole.

FIG. 4 is an example of an auricular extrasystole. The radial tracing shows the abortive ventricular beat, the venous tracing presents an unusually early *a* wave, which is followed by the premature *c* wave. At times the *a* wave may come so early as to coincide with the *v* wave of the preceding cycle, at which times it is often unusually high. The impulse for the auricular extrasystole has its origin in some other portion of the specialized auricular tissue than the sinus.

The auriculoventricular extrasystole takes its origin from the node of Tawara. In this form the auricle and ventricle contract simultaneously. It is a more difficult form to identify from the polygraphic tracings than the other two.

So far the exact value, from a clinical point of view, of the differentiation of the three varieties of extrasystole, has not been definitely determined, but it seems very likely that with a more complete understanding of the subject this will be developed.

**THE PATHOLOGY OF EXTRASYSTOLE.** Extrasystole evidently occurs because of an increased irritability of the specialized cardiac tissue (primitive tube of Mackenzie) so that impulses are received from other points than the sino-auricular node. The pathological lesions when present are of the sclerotic type, hence the condition is most often seen in those who suffer from arteriosclerosis or where there are fibroid changes in the heart from other causes, such as rheumatism. It may be seen at any age, though it is, of course, more common in those past middle life. There seems to be a growing tendency to consider extrasystole an evidence of serious

change in the heart muscle, in spite of the fact that experience has taught us that in many instances it may be present for long periods without other signs of heart disability. Gastro-intestinal disturbances are not infrequently the cause of extrasystole, as is also the excessive use of tobacco.

There may or may not be subjective symptoms of this disorder. Some patients are entirely oblivious to the abnormality, while others are greatly annoyed by a fluttering sensation in the region of the heart or they complain of the violent throb which follows the long pause; some have a sensation of great weakness when the heart is intermitting. Some in fact become so disturbed and nervous that they are almost typical neurasthenics. Medication directed toward the correction of this disorder is very unsatisfactory. The underlying cause must be sought.

**HEART-BLOCK (PARTIAL OR COMPLETE).** This form of irregularity is much less common than those just described, and is due to a disturbance of conductivity. The impulse which starts at the sino-auricular node may be delayed or entirely obstructed in its progress to the rest of the heart, resulting in partial or complete heart-block. The interruption may take place at the sino-auricular or at the auriculoventricular junction, and, according to some, at the interventricular junction (dissociation of the ventricles). The most usual and most important of these is the auriculoventricular heart-block which may be either functional or organic. Functional block, as a rule, results from excessive doses of drugs of the digitalis group. This accident, however, is much more likely to happen in cases where the bundle of His is diseased. Organic block is due to disease of the bundle of His or the tissue immediately surrounding it. The common causes then are sclerotic changes in the coronaries with the usual results or old rheumatic inflammation. Rarely, however, the bundle of His may itself be the seat of a growth such as gumma, or may be pressed upon by such a tumor. The first indication of heart-block is a lengthening of the *a-c* interval (the time between the appearance of the *a* wave and the *c* wave in the venous tracing, see Fig. 6). In other words, the ventricular contraction does not follow the auricular as soon as it should. This lengthening of the *a-c* interval may be for a long time the only evidence of interference in conduction, then the impulse may from time to time fail to get through, resulting in the dropping of a ventricular beat. This may occur at regular or at irregular intervals, and if the block becomes complete, the ventricle assumes its own rhythm which is much slower than that of the auricle. It is in these cases that the Stokes-Adams syndrome is observed.

In organic heart-block the prognosis is necessarily grave, though there are cases on record which have lived for a number of years after the development of the condition. Of course, the cardiac

capacity is reduced in proportion to the degree of block. The functional cases usually recover promptly on the removal of the cause. In those rare instances where the symptoms result from the effects of a gumma upon the bundle of His, antiluetic treatment may be resorted to with some hope of success. It is easy to see that the use of digitalis in cases of heart-block might be fraught with great danger because of its tendency to delay transmission of the impulse from the auricles to the ventricles. James MacKenzie,<sup>9</sup> however, makes the following statement: "The presence of heart-block is not necessarily a contraindication to the use of digitalis. When it is complete it cannot interfere with the conduction of the *a-v* bundle, for conduction is abolished, and so far there is no evidence that digitalis has any effect on the idioventricular rate." Drugs of this group would certainly appear to be contraindicated where there is a tendency to heart-block, and, if used at all, it should be with the greatest caution.

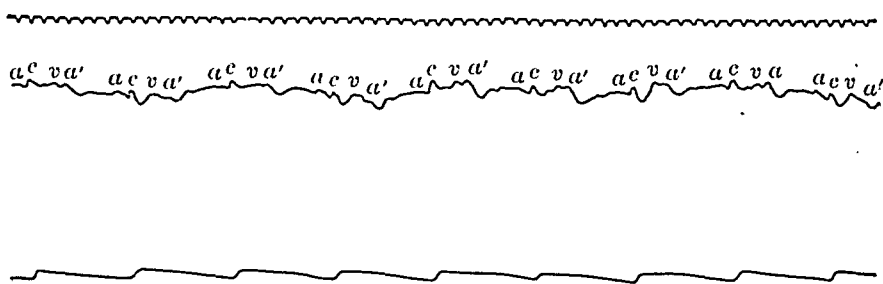


FIG. 5.—Polygraphic tracing from a case of 2 to 1 heart-block. Radial pulse about 37 to the minute. The *a'* waves are auricular contractions which were not followed by ventricular contractions.<sup>10</sup>

Fig. 5 is from a case of heart-block of the 2 to 1 type, the history of which is briefly as follows:

H. B., white male, aged forty-seven years, married, a manufacturer. His parents had been long-lived, and his own health, when a young man, had been excellent. When aged twenty-seven years, he became infected with lues, which was not treated for six months. He then became quite ill and the real condition was recognized, when he received proper medication for a few months continuously, and for years, off and on, for the disease continued to manifest itself from time to time. At thirty-five he had typhoid fever severely. He then enjoyed good health until he was forty-one, when he had several fainting attacks. There was no special discomfort, simply temporary loss of consciousness. At this time a heart murmur was discovered, but there were no symptoms

<sup>9</sup> Heart, 1911, No. 4, p. 293.

<sup>10</sup> In other portions of Tracing No. 5 where the radial diastolic notch came out clearly it could be satisfactorily demonstrated that the *a* waves were no part of the *v* waves.

of cardiac insufficiency, unless the attacks of syncope were to be attributed to this cause. When aged forty-five years he had an attack of either la grippe or rheumatism (it was difficult from his description to say which), but during the illness heart symptoms developed, and three months later swelling of the feet and dyspnea. During this attack he had peculiar fainting spells. There would be what he described as a rushing sensation from the heart to the head and then unconsciousness lasting from one to five seconds. There was usually time for him to reach the bed or a chair before he would faint, but not always. The heart seemed to stop at the time of the seizure. At times vomiting of blood with great weakness followed. On examination the heart was found to be slightly enlarged, a systolic murmur was heard all over the precordia, with maximum intensity at the apex and transmitted to the axilla. There was also a diastolic murmur heard all over the precordia, the second aortic was faint, and the second pulmonary accentuated. The diastolic murmur was not a typical aortic insufficiency murmur or did the radial tracing conform to the type of that lesion.

Unfortunately I was only able to observe this interesting case for a few days, as he was a transient. A Wassermann reaction was negative, and as there is some doubt as to the advisability of the use of salvarsan in those suffering from severe heart lesions, I hesitated to administer that preparation, but I advised a course of mercurial injections, and my patient went to his home with the avowed intention of returning for treatment, but as yet I have heard nothing from him.

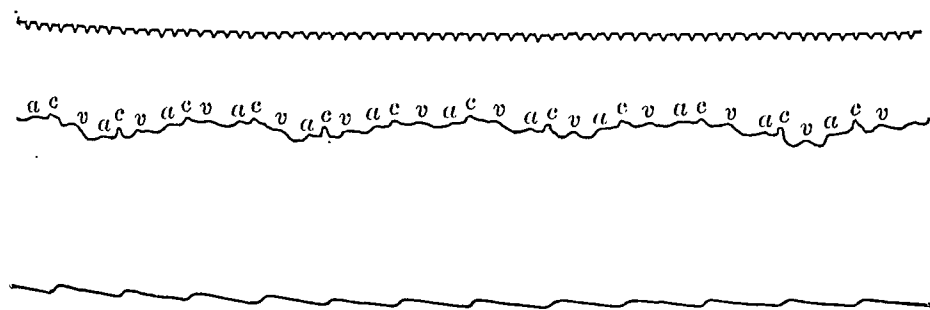


Fig. 6.—Polygraphic tracing taken between attacks, from the case of heart-block here reported. Delay in the *a-c* interval may be noted in several places upon the tracing. Pulse rate about 60 to the minute.

The attacks which had preceded the one in which I saw this man had been of brief duration, the heart maintaining the slow beat but a few hours or a day at most. This attack, however, kept up for several days, with only short intermissions. He had discovered that a strong drink of whisky would, for a time at least, bring the pulse up to normal. I saw this verified (Fig. 6). During the period of slow ventricular action the patient was able to walk only at a very slow pace, and had to be very careful not to over-

exert himself in any way, yet he travelled about alone, attending to his business affairs.

**AURICULAR FIBRILLATION (THE WHOLLY IRREGULAR PULSE).** This is characterized by an entire loss of the sinus or fundamental rhythm, the beats are irregular both as to time and as to volume. In the venous tracing the auricular wave is missing, in other words, there is no auricular contraction, the venous pulse being of the ventricular or positive type (Fig. 7). There is a general fibrillary contraction of the auricular muscle, but no contraction of the muscle in mass. The electrocardiogram shows an absence of the *P* wave (auricular contraction), and by a series of fine undulations that there are a number of impulses at the rate of four to nine hundred a minute trying to get through to the ventricle. Of course

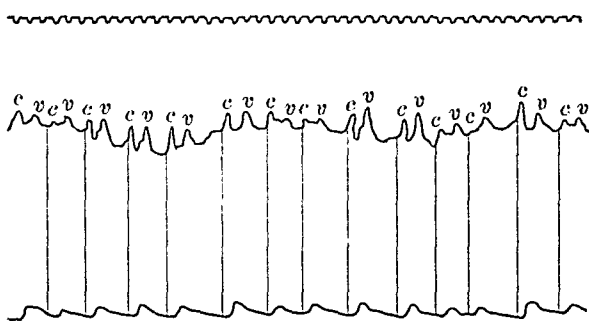


FIG. 7.—Auricular fibrillation. Note absence of *a* wave and irregularity as to time and volume of radial pulse.

the ventricle is entirely unable to respond to anything like this number, and hence responds only as it may, which results in absolute irregularity. Where a mitral presystolic murmur has been present it disappears as might be expected; it being produced during the contraction of the auricle.

**PATHOLOGY OF AURICULAR FIBRILLATION.** The heart muscle as a whole shows a more or less marked grade of inflammatory change resulting in fibrosis. The morbid changes are said to be particularly marked in the auricular tissue, especially at the sino-auricular junction; the same changes have been noted at the auriculoventricular bundle and in scattered areas of the ventricular musculature. Though these very decided changes have been noted in cases of auricular fibrillation, just the same conditions have been found where, during life the rhythm had been normal.

It is in this form of irregularity that digitalis has been found of the greatest value. It apparently acts by cutting down the number of contraction impulses which get through to the ventricle. The prognosis should be guarded in these cases.

**THE PULSUS ALTERNANS** is not properly a disorder in the cardiac rhythm as the time between the beats is the same in uncomplicated

cases, but it is not unusual to note the condition in combination with other forms of irregularity such as extrasystole.

This form of irregular pulse is seen clinically under two sets of circumstances, namely: (1) When the apparently healthy muscle is overtaxed, especially when the rate is unusually rapid, as in tachycardia, and (2) when the musculature is profoundly affected, usually by the senile changes. It is said that in those of the second class it is frequently accompanied by grave symptoms, such as pain of an anginal nature, and those who show alternation are not likely to live more than a few years. As a rule the blood pressure is high.

In conclusion I would say that the graphic study of the pulse is not only interesting to any one who will give it sufficient attention, but, in many instances, facts of importance may be learned from it. It would be extremely difficult to positively identify some sinus arrhythmias in any other way than instrumentally, and yet this might be of vital importance. There are also cases of extrasystole which could not be distinguished from auricular fibrillation by the usual methods of physical examination. A delay in the *a-c* interval may be the first indication of an impending heart-block, and when a block is actually established, none but the experienced observer would be able to identify it without instrumental assistance. As our knowledge of the causes of the individual irregularities becomes more exact, it seems fair to suppose that it will become increasingly important to be able to recognize and give them their true valuation.

While no specific reference has been made in the text of this article to Thomas Lewis' book, *Mechanism of the Heart Beat*, it is a most complete collection of the data bearing upon the whole subject as well as embodying many original observations, and is of inestimable value to those who may be interested.

---

## CRYPTOGENETIC GRANULOMATOSIS OF THE STOMACH.

BY O. C. GRUNER, M.D.,

AND

E. J. MULLALY, M.D.,

MONTREAL, CANADA.

(From the Pathological Laboratories, Royal Victoria Hospital, Montreal.)

EXTREME thickening of the walls of the stomach, with marked shrinkage of the organ, has been observed frequently, and has received a different name at the hands of every writer on the subject. The attempt has been made to class every example of

this type of disease under the one heading, "cirrhosis of the stomach" or "linitis plastica," regardless of the fact that the microscopic anatomy of the condition is not always the same. The most recent contribution on the subject is that by Henry H. M. Lyle,<sup>1</sup> who classifies the cases in the literature into benign and malignant. Some of the latter cases were characterized by the presence of "epithelial" cells lying in meshes of undulating connective tissue fibers in the submucosa, infiltration of the submucosa with fusiform cells, and endarteritis in the vessels. Lyle admitted that it was a disputed question whether these epithelial cells were really carcinomatous or whether they sprang from the endothelium lining the normal lymph spaces. In view of the changes that were noticed in 2 of our series, the fact that the adjoining lymph-nodes were usually fibrosed in Lyle's collection leads us to doubt the correctness of the view that such types of disease are necessarily malignant. Four specimens which have come under the writers' notice demonstrate the existence of certain histological types of the disease and corroborate the results of an investigation of the literature of the subject from this standpoint. It seems possible, accordingly, to classify the cases into the following three main groups: (1) Definitely cancerous cases; (2) pre-cancerous or doubtfully cancerous cases; (3) non-cancerous cases. It is the purpose of this paper to present the evidence in favor of the classification submitted.

CASE I.—Definitely cancerous. J. P., male, aged forty-eight years. Had symptoms pointing to cancer of the stomach. The autopsy showed an extensive cancer in the stomach with multiple discrete nodules scattered through it. The tissues around were infiltrated.

Histologically the mucosa and submucosa were replaced by large branching acinous masses of cells of epithelial type, separated from each other by only a scanty amount of fibrous tissue. The muscularis was not infiltrated, the carcinomatous cells spreading uniformly along the thickened walls of the stomach without passing through to the peritoneal side. Apart from the rarity of the mode of invasion of the gastric wall, the case presents no striking interest because the histological diagnosis is easy and allows of no alternative opinion.

CASE II.—E. S., male, aged forty-seven years, had suffered from epigastric pain and vomiting for six months. Vomiting came on seven weeks before admission to hospital. There was blood in the vomited matter. Liquids alone were retained. There was much emaciation.

The stomach was excised. It was a small organ, about 15 cm. in length, with uniformly thickened walls. The patient did not



survive the operation longer than one week. The autopsy showed bronchopneumonia with extensive consolidation. There was a little peritonitis at the site of operation, and there were no infected glands.

**Histological characters:** The gastric glands are intact but their fundi are obscured by an excessive amount of small round-celled infiltration which spreads as far as the well-marked narrow stratum of muscularis mucosæ. Between this and the muscularis is a striking amount of submucosal infiltration (1.4 cm. in thickness). The muscle fibers of the muscularis are separated by a very dense cellular infiltration of the same type as is seen in the submucosa, and a similar change extends through to the peritoneal coat, where there is a layer of organizing granulation tissue. In one portion of the sections there are small tongue-like acini of cuboidal cells which simulate spheroidal-celled carcinoma. These occur immediately beneath the muscularis at the extremity of the section.

**Characters of infiltration:** The cells are large and polygonal; the cytoplasm is narrow; the nucleus is oval, pale, and finely granular in structure. Some cells are provided with a very pale structureless nucleus, while some have a broader cytoplasm. The cells are mostly of one type, and are *mesolymphocytar* in character. They are separated by strands of fibrous tissue at long intervals. Here and there the fibroblastic infiltration is diffuse and marked. There are very few true lymphocytes, but there are a number of lymphocytar cells mixed with eosinophiles of histiogenic type. Occasionally there are mitotic figures in the lymphoidocytar cell-types. Some of the eosinophile cells have the character of micromyelocytes. The exudate between the tubules consists very largely of cells of mesolymphocytar type intermingled with a number of plasma cells of the ordinary form. There are many other forms present, such as small lymphocytes, lymphoblasts, and myelocytiform cells. The plasma cells are most numerous near the orifices of the glands and here eosinophiles appear. There are some small, fairly well outlined lymphoid nodules just beneath the mucosa.

**CASE III.**—A. P. L., male, aged fifty-two years. Had suffered from epigastric pain for years. Latterly he had been much worse and was now unable to retain solids. He had had ague twice, and admitted gonorrhea, but not syphilis. There was a small mass in the epigastrium. The test-meal showed absence of free HCl. The autopsy showed extreme emaciation, strong basal pleural adhesions on both sides, atheroma of the cerebral arteries, but not of the aorta. There were miliary nodules over the peritoneum, and there was ascites. The glands in the portal fissure and mesentery were enlarged. The kidneys were very cystic. The stomach was not dilated; its walls were uniformly and markedly thickened

( $\frac{1}{2}$  inch) from the cardiac end to within an inch of the pylorus. There was a small ulcer near the pylorus. The testes were normal.

Histological characters: The submucosa is occupied by a very edematous and cellular tissue. The gastric glands are just visible here and there, but are much obscured by the degree of cellular infiltration between them. The individual cells are considerably separated as if from catarrh. The submucous tissue contains a number of polymorphous cells with oval pale nuclei and scanty chromatin network. The cell body is very large and pale. Among them are small lymphocytes and a few plasma cells of ordinary type. There are many binucleate and trinucleate eosinophile cells. Running irregularly throughout the whole are some broad, absolutely ill defined bands of hyaline substance. The bloodvessels are scanty. This condition goes down almost uniformly to the muscularis, but the cellular content is increased as one passes in that direction. The cellular infiltration is very dense among the muscle fibres; it does not seem to displace them much. On the peritoneal side there is little or no deposit, though there are flattened delicate spindle cells running along in the form of a thin band covering the muscularis. The nodule on the peritoneum shows a loose structure of elongated spindle cells, a few polymorphs, and much edema. There is no evidence of carcinomatous change in it.

CASE IV.—G. P., female, aged sixty-two years. Had symptoms pointing to carcinoma. The autopsy showed a leather-bottle stomach and infiltration of the adjacent coils of intestine by new growth, with consequent stricture of the lumen of the intestine. There were miliary nodules over the peritoneum.

Histological characters of the tissue: The submucosa is occupied by a very cellular tissue containing delicate connective-tissue fibrillæ running through it in all directions and leaving minute spaces in which lie the individual cells composing the tissue. These cells are medium in size, round or polygonal in shape, and have a regularly large oval nucleus with scanty nuclear markings, very amblychromatic and very clearly defined nuclear membrane. Some of the cells have an eccentric nucleus of small size. Very few elongated nuclei occur, showing that there is little tendency to differentiate into young fibroblasts. One or two very large cells occur with relatively preponderating cell-body. This infiltration becomes a little fibrous as one approaches the muscularis. There is very little involvement of the latter and little increase of fibrous tissue. On the peritoneal side is a little exudate which is moderately cellular, the cells being of a different type, pale, and far apart, and of more spindle shape (broad body and oat-shaped nucleus). There are a few scattered lymphocytar cells. The bloodvessels are very congested. Here and there are a few thromboses, and, in a few areas, hemorrhages occur. Another section

shows a very decided fibrosis in the submucous layers. The glandular layer cannot be seen. A third section shows some edematous portions with very wide separation of the cells, though these are relatively more numerous. Some of the larger cells appear to be vacuolated and others show mitotic figures, and others (looked at from an impressionist point of view) may be regarded as bearing some resemblance to carcinoma cells.

CASE V.—G. B., male, aged fifty-six years. Had symptoms indicative of gastric carcinoma. The autopsy showed a diffuse thickening of the gastric walls with shrinkage of the organ. No other abnormal points were noted.

Histological characters of the tissue: The wall of the stomach is entirely occupied by new tissue. There is a small relic of muscular tissue. The mucosa itself is replaced by cellular tissue which is very thick (1.5 cm.). In one or two places there are some thick-walled bloodvessels, but the bulk of the tissue is almost avascular. There are irregular strands of fibroblastic tissue which vary in thickness. Here and there in this tissue there are just sufficient spindle cells to give it a fibrous appearance, otherwise it consists of necrotic or fibrotic interstitial substance in which lie large round discrete cells with very trachychromatic nuclei and relatively scanty dusky basophile cytoplasm. Among these there are a few very large cells with lobed nuclei simulating the metrocytes found in bone-marrow. Others have a more oxyphile cytoplasm with a nucleus in which no structure can be discerned. Many examples are in a state of amitosis. In addition there are cells of the size of mesolymphocytes with a relatively scanty cytoplasm. A moderate number of small round cells like ordinary lymphocytes can be seen. Necrotic areas occur here and there. They are small, irregularly shaped, and contain a few fragmentary nuclei of punctate form up to the size of an ordinary lymphocyte nucleus. These areas strongly recall those seen in acute streptococcic infections. In between the strands referred to there are ill-defined collections of small round cells which are separated by a more or less abundant reticular connective tissue and include very many densely trachychromatic lymphoid cells. A few larger cells occur here and there, presenting a type of plasma cells. Eosinophiles are not noted at all.

A second section shows patchy infiltration between the muscular bundles, and the tissue is everywhere looser in texture. Short spindle-shaped cells and small round and polygonal cells being intermingled with the larger cells of the types described above. Many lines of fibrous tissue are more conspicuous here than in the other section. A few cells occur which contain cell-inclusions.

The last of these cases appears to be essentially distinct from the others, the difference consisting in the abundance of large, atypical, uninucleate giant cells which occur in groups through the

tissue. These groups are not acini but are collections of cells which have no very definite relations with each other and are of an endothelial type, suggestive of their connection rather with fibroblastic metaplastoid tendencies. We have not found more than one case in the literature, either in the references presented by Lyle or in certain other references quoted at the end of this article, which is at all comparable with the particular condition which we have classed at the outset as non-cancerous.

This case is reported by Johnston,<sup>2</sup> and occurred in a boy, aged thirteen years, who only weighed thirty-seven and one-half pounds. The stomach measured 5 by 2.5 cm., and its walls were free from 0.8 to 1.5 cm. thick. There was general lymphadenitis. There was a small ulcer at the pylorus. The mucosa was everywhere lost except toward the pylorus, where fragments were still discernible. The muscle fibers were separated by vascular connective tissue, in which there was a variable amount of small round-celled infiltration. Among these inflammatory cells plasma cells were noted in abundance. Ganglion cells were numerous in the walls of the upper portion of the stomach but less numerous in the lower portion. These cells were large, and occurred in groups and were surrounded by connective tissue, and took a darker stain than the surrounding cells. There was no evidence of carcinoma anywhere. The vessels were frequently plugged by thrombi. The peritoneum was uniformly thickened over the ulcer and there was marked round and plasma cell infiltration of all the tissues of the wall at this spot as far as the peritoneal surface. There were no pathological changes in the wall of the duodenum.

The character of the tissue itself is quite characteristic; it has all the indications of granulation tissue of chronic type. In other words, an observer, not knowing the source of the tissue, would suppose it to be a granulomatous mass similar to that produced by mycotic infection. The peculiarity is that the change has extended uniformly along the whole organ. Those who, with Krompecher, regard the condition as secondary to a chronic venous stasis provide an explanation for a chronic toxic agent, acting over a long period of time, stimulating the connective tissue cells to multiply in this fashion. Granuloma formation elsewhere is attributable to a toxic agent acting over a long period of time.

According to Boas,<sup>3</sup> the cirrhotic condition of the gastric wall is due to chronic spasm of the muscles. Such an explanation is rarely borne out by the microscopic characters of the muscular coat.

Much depends on the interpretation which is to be placed upon the so-called epithelial cells. Where they occur diffusely and intermingle without fibrous boundaries with inflammatory cells of all kinds, such as occur in a chronically inflamed tissue or a

<sup>2</sup> Trans. Chicago Path. Soc., vi, 336.

<sup>3</sup> Deutsch. med. Woch., 1902, p. 170.

healing or organizing granulation tissue, they are probably really nothing more than hypertrophic or actively multiplying connective-tissue cells or adventitial cells, and are not at all neoplastic in nature. It is only in those cases where they form definite acini demarcated by a capsule of more or less well defined fibrous tissue that the diagnosis of carcinoma can be maintained. The occurrence of a few packets of cells, unless they present very characteristic cytological features, cannot be held to be conclusive of malignancy. The similarity to this type of cell, which is presented by the hypertrophic ganglion cells in the gastric wall, is also very suggestive of error having arisen in the description of certain cases.

For these reasons we would be disposed to assume that in some of the doubtful cases of the literature, for example, Stretton,<sup>4</sup> Grooves,<sup>5</sup> Nuthall and Emanuel's,<sup>6</sup> Kussmaul's and Schirren's, we have before us examples of the third type of cirrhosis of the stomach, that which simulates granulomas of known etiology. In the present instance, as especially exemplified by the fifth case which we report, the similarity to some other granulomas of other obscure origin, would make it suggestive to place it in a similar group. Since its etiology is unknown, though probably toxic in nature (not syphilitic) it may be called a cryptogenetic granuloma. Since the condition is diffuse the term granulomatotic hyperplasia better describes the appearances, and emphasizes the diffuse character of the disease. Furthermore, this enables the local type of cirrhosis of the stomach to be excluded from the classification because the thickening is here due to pure fibrosis without the occurrence of any small-celled infiltration; for example, Tilger's<sup>7</sup> case.

As regards the relationship of the granulomatous change to carcinoma, it may be pointed out that the presence of a few acini of apparently cancerous cells, in the midst of or at the edge of a massive inflammatory tissue, hardly justifies the conclusion that linitis plastica is primarily malignant. There is no reason why a small nodule of spheroidal-celled carcinoma in one spot, generally near the pylorus, should excite a widespread fibrosis extending along the whole surface of the stomach. A similar condition is unknown in any other part of the body. The analogy to the carcinomatous change appearing in a lupus or in a tongue along the seat of chronic interstitial syphilitic glossitis is suggestive. On the other hand, it is not possible to state that Case V would not have developed cancerous acini if life had been prolonged.

The fact that some of these cases have been described as sarcoma brings up the problem of lymphosarcoma versus lymphogranuloma, a problem which has arisen in connection with new

<sup>4</sup> Lancet, 1909, p. 465.

<sup>5</sup> Trans. Path. Soc., London, 1903, p. 90.

<sup>6</sup> Practitioner, 1905, lxxv, 172.

<sup>7</sup> Virchow's Archiv, Band cxxii, p. 290.

formation of tissue in other parts of the body. According to Naegeli,<sup>8</sup> Ribbert,<sup>9</sup> and others, the formation of a lymphosarcoma, resulting from purely parenchymal hyperplastic processes, is distinct from the formation of a granuloma where there is an interstitial proliferation associated with the parenchymal change. The other school of hematologists, following Pappenheim,<sup>10</sup> bring these processes into closer relation by regarding them both as variants of lymphosarcomatous development. It is more satisfactory to look upon these processes as related in this latter way, because it affords an explanation for the possible change between the one form of disease and the other. The noxa which stimulated the abnormal proliferation of potentially hematopoietic cells may or may not also irritate the purely stromatic cells and lead to the histological picture of a lymphosarcoma or of a granulomatous tissue (one form of linitis plastica) respectively. The view that it is an irritant which starts the whole process renders it more intelligible why one should meet with cases which run diffusely through the gastric wall alone, and sometimes with cases which run through the intestinal walls as well. From the description of such cases as are available it is impossible to escape the conclusion that the so-called "diffuse carcinoma" is really a form of lymphosarcoma with more or less conspicuous involvement of the purely connective-tissue cells. A good example of the purely lymphosarcomatous hypertrophy of the gastric wall which was very extensive though not general through the whole stomach was reported by one of us<sup>11</sup> recently, and brings out the contrast between the two conditions as well as a demonstration of the possible interchangeable character of the lesions according to the preponderance or otherwise of the interstitial hyperplastic phenomena. This possibility is further shown by those few cases of "malignant granuloma" which have occurred in this hospital during recent months, where there was in addition a megakaryocytar hyperplasia with the production of a very characteristic histological picture.

The introduction of these three forms of disease in a commentary on the cases of linitis plastica which are in question serves to explain the view that each of these three processes may represent different modes of action of one group of etiological factors. The view that slightly different histological manifestations can result from one and the same causal agent has been advanced by Pappenheim, in 1909, who gave arguments for believing that a toxic infective agent could set up granulomatous and leukemic processes on the one hand and lymphosarcomatous processes on the other, and that some lymphosarcomatous growths could arise under different conditions still, conditions in which an infective agent had no part.

<sup>8</sup> Blutkrankheiten, 1908.

<sup>9</sup> Allgemeine Path., 1909.

<sup>10</sup> Folia Hæmatologica, 1907, pp. 244 and 246.

<sup>11</sup> Gruner, Canadian Pract. and Rev., March, 1912.

To summarize the ideas above expressed, in so far as they bear upon the linitis plastica, we arrive at the conclusion that this disease is not a new kind of morbid process, but is the effect of some chronic infective agent whose nature has not yet been determined. The process at work is often akin to the granulomatous process which occurs in mediastinal tissues and elsewhere, it is akin to the changes which occur in the course of some forms of tuberculosis and of diffuse sclerotic types of tertiary syphilis, and it is occasionally followed by the development of an epithelial growth, just as is sometimes noticed as a sequel to tuberculosis and syphilitic lesions.

The disease known as linitis plastica, or cirrhosis of the stomach, only demands a separate name because it is clinically a simulator of true carcinoma. Its prognosis should be more favorable and its treatment by the surgeon more effective.

It is further worthy of mention that the small degree of epithelial overgrowth which may be regarded by some observers as carcinomatous, in Cases II, III, and IV of our series, are not really any greater in extent than are the atypical proliferations of epithelium which are known to result from the subcutaneous introduction of certain irritant lipoid soluble bodies. The suggestion is that the abnormal cells in this granulomatous tissue are pouring out substances which may excite the overgrowth of the glandular epithelial cells in the same way that many bodies (dimethylamidoazobenzol, amidoazotoluol,  $\alpha$ -naphthylamine, methylimidazol, indol, and skatol, etc.) were found to excite epithelial overgrowth by Wacker and Schmincke<sup>12</sup> in 1911. This renders the development of carcinoma as a secondary process on a preëxisting (often long-persistent) submucosal disease quite intelligible, and emphasizes the view which we would point out that the malignant change in this, as in "Hodgkin's disease," and in many lymphosarcomas (also in Paget's disease of the bones), is not an inevitable sequence, but is superimposed by the succumbing of certain other tissues to the continued noxious action of abnormal cell-products.

---

## THE ALIMENTARY HYPERSECRETION OF CHRONIC ULCER AS SHOWN BY THE LACTOSE TEST MEAL.<sup>1</sup>

By DUDLEY ROBERTS, M.D.,

ATTENDING GASTRO-ENTEROLOGIST, BROOKLYN HOSPITAL; CONSULTING GASTRO-ENTEROLOGIST,  
CONEY ISLAND HOSPITAL AND KING'S PARK STATE HOSPITAL, BROOKLYN.

CONSIDERABLE data must be collected before the causation of anomalies of gastric secretion will be entirely understood. Much

<sup>12</sup> Münch. med. Woch., 1911, p. 1607.

<sup>1</sup> Read before the American Gastro-enterological Association, June 3, 1912.

of the literature on the subject was written when clinical pictures were differently interpreted from the way they are today. The relation between stomach symptoms and diseases of other organs was little appreciated previous to the present decade. Chronic peptic ulcer was an almost unknown disease. Methods of diagnosis have gradually been improved, and entirely new methods have been originated.

The literature concerning gastric secretion following the ingestion of test meals is meager and unsatisfactory. With the ordinary test-meals in vogue it has been impossible to gain any notion of the constitution of extracted chyme. As a routine, we have been most concerned with the presence and percentage of free acid and the total acidity. Sahli and Friedman have each proposed a test-meal containing fat which was to be used as an index of the amount of the chyme made up of test-meal residue. Little clinical work with these methods has been reported.

Last year at the meeting of the American Gastro-enterological Association, I urged the advantages of a test-meal in which lactose was used as an indicator. Let me briefly recall the composition of this meal and its method of use, referring to the original article<sup>2</sup> for necessary details. The test meal consists of 300 c.c. of weak tea or water to which is added 30 grams of lactose. With this the patient takes two unsalted, unsweetened crackers. At the end of an hour a portion of chyme is extracted, and then a definite amount of water, for example, 150 c.c., is injected through the tube and mixed with the chyme by partially withdrawing it and forcing it in again. From the difference in the acidity of these two samples the total stomach content is calculated by the formula suggested by Mathieu. The lactose percentage is then accurately determined in the first or undiluted specimen, and from that we determine the amount of sugar remaining in the stomach, and calculate the amount of the chyme which is made up of test-meal residue, and that which is made of gastric secretion.

During the last year I have continued the daily use of this test-meal, and have been convinced of its accuracy and the importance of the obtained data. Repeated tests in the same individual show that the results are consistent. Its accuracy in the estimation of the motor power of the stomach has been corroborated by Röntgenoscopy when used as an aid to diagnosis. In no thoroughly studied case have we been able to contradict that it gives an accurate idea of the motor power of the stomach for fluids. The question arises as to the accuracy of estimation of gastric juice secretion. Unfortunately, we are lacking in practical methods to verify the results, but from our studies we have no reason to question their accuracy.

<sup>2</sup> Jour. Amer. Med. Assoc., March 16, 1912, lviii, 753.



We know how much test-meal has passed out of the stomach from what remains, and the question remains as to whether a proportionate amount of gastric juice has passed over. This problem is difficult of solution, as we have no means of knowing that in the hour of the test conditions are at all times the same as when an hour has expired. In the same case, tests taken at periods after the ingestion of the test-meal, varying from ten minutes to one hour, indicate that gastric secretion begins promptly after this test-meal; free acid is soon present, and even in ten minutes the stomach may contain from 50 to 100 c.c. of gastric juice. If it be true that the rate of gastric juice secreted and passed from the stomach corresponds proportionately with the test meal evacuated, there must be wide deviations in the amount of secretion, and, in certain cases, the amounts must be very great. This is a matter of much practical interest.

An idea of the amount of secretion is gained by the ratio which obtains between the test-meal residue and the gastric-juice residue. Thus, if we find 50 c.c. of test meal and 100 c.c. of gastric juice in the stomach, the ratio is 1 to 2. If the rate of exit of the two is constant, then, using the same example, the amount of gastric juice passed out would be 250 times 2 or 500 c.c. of secretion passed and 100 remaining. These figures are not surprising when we stop to think how large is the amount of gastric juice produced by a fractional part of the canine stomach, studied with the Pawlow method.

In order that we may appreciate the results obtained in chronic ulcer, it will be necessary first for us to fix in mind the figures for cases which have been selected as normal and those where certain definite conditions have been discovered other than the one under consideration. A large number of cases have been studied in search of possible gastric derangements and for statistical purpose. From these I have selected 10 which appeared to be within the normal limits of motility and secretion. Not every case, experimentally studied, proved to be as normal as its freedom from complaints might seem to indicate. This is, it seems to me, a thing we should expect.

TABLE I.—Normal Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	19	40	30	47	1 to 1.6
2	34	55	33	80	1 to 2.4
3	20	60	34	50	1 to 1.5
4	30	50	35	81	1 to 2.2
5	32	47	45	85	1 to 1.8
6	16	54	29	80	1 to 2.8
7	32	44	24	41	1 to 1.7
8	20	40	26	31	1 to 1.2
9	30	50	35	80	1 to 2.3
10	10	41	50	97	1 to 1.9

There is little use in prolonging this table for normal cases, as the standard is necessarily more or less arbitrary. I regard the above figures as within the normal limits. We may say that more than 50 c.c. of test-meal residue shows deficient motility, and that the ratio of test-meal residue to gastric-juice residue should be about 1 to  $1\frac{1}{2}$ . If the two are equal, or the gastric juice less than the test meal, there is deficient secretion. I would not place the upper limits of this ratio with an equal degree of positiveness. The question presents itself as to whether symptoms or pathological digestion arise, as a rule, when the ratio reaches a certain figure. It will take a deal of study and clinical observation to determine such questions.

TABLE II.—Enteroptotic Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	18	42	84	60	1.4 to 1.0
2	10	35	85	68	1.4 to 1.0
3	16	42	123	41	3.0 to 1.0
4	8	28	216	150	1.4 to 1.0
5	9	26	191	104	1.8 to 1.0
6	34	60	15	44	1.0 to 2.8
7	30	50	57	76	1.0 to 1.3
8	0	12	205	195	1.1 to 1.0
9	0	18	40	30	1.3 to 1.0
10	0	12	34	48	1.0 to 1.3
11	10	26	62	102	1.0 to 1.7
12	0	12	32	48	1.0 to 1.5
13	30	46	47	47	1.0 to 1.0

In order to give some idea what takes place in the general group of cases spoken of as enteroptotics we have compiled Table II. It is apparent that in the main these cases are characterized by some degree of motor insufficiency. In some cases the motor capacity for fluids is fair or even excellent. In quite a large proportion the secretion is low. In this type of case it rarely appears high. Case 8 in Table III is shown to have a fair degree of hypersecretion. In this case there was a marked enteroptosis.

TABLE III.—Chronic Appendicitis.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	22	41	75	105	1.0 to 1.4
2	60	76	25	86	1.0 to 3.2
3	12	32	85	60	1.4 to 1.0
4	20	44	75	106	1.0 to 1.4
5	34	60	59	103	1.0 to 1.7
6	50	65	51	120	1.0 to 2.3
7	20	35	28	84	1.0 to 3.0
8	44	64	43	75	1.0 to 1.7
9	12	30	101	80	1.2 to 1.0
10	0	18	40	33	1.2 to 1.0

These cases were all explored and the sole lesion was a chronic appendicitis. In Cases numbered 1, 6, 7, 8, there was epigastralgia of severe grade which ceased after appendectomy. From the marked difference in the degree of acidity and gastric juice in these cases it would seem doubtful that the acid secretion caused the pain, either directly or through inducing pylorospasm. In Cases 2 and 8 there was hunger pain relieved by alkalis and the ingestion of food. The high secretion in these cases may have been a factor in the causation of the discomfort.

TABLE IV.—Gall-bladder Diseases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	30	50	80	90	1.0 to 1.1
2	44	72	31	67	1.0 to 2.2
3	28	40	211	142	1.6 to 1.0
4	0	15	65	65	1.0 to 1.0
5	0	13	112	53	2.0 to 1.0
6	38	51	57	84	1.0 to 1.4
7	8	32	33	44	1.0 to 1.3

Gallstones were found at operation in the first 3 cases. In the other 4 considerable observation has justified a positive diagnosis of gall-bladder trouble, but operation has as yet been refused. Test-meal studies have not been necessary in the majority of our cases, as the diagnosis was sufficiently clear to allow the recommendation of operation unhesitatingly. In the cases reported the nature of the complaints was such as to make differential diagnosis between a gall-bladder disease and other abnormal conditions somewhat difficult. The results of the test meal were of great value in reaching conclusions, particularly in Cases 1 and 3. Here there was epigastric hunger pain relieved by food. In Case 3 there was a hematemesis after prolonged vomiting, but exploration showed no ulceration.

TABLE V.—Ulcer Cases.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
1	56	80	36	149	1 to 4.0
2	66	80	34	136	1 to 4.0
3	46	68	55	224	1 to 4.0
4	44	65	20	150	1 to 7.0
5	36	50	37	130	1 to 3.7
6	46	60	64	212	1 to 3.4
7	80	120	15	138	1 to 9.0
8	38	50	38	119	1 to 3.2
9	36	61	10	94	1 to 9.4
10	20	44	36	139	1 to 3.7

It is obvious that in this group of cases there is a decided tendency to alimentary hypersecretion. (There is the question of the correctness of the diagnosis, sometimes admittedly a difficult

matter.) Only the first 2 cases have been submitted to operation, and in both there was duodenal ulcer. In Cases 4 and 5 there could be no doubt of the diagnosis, as there was marked overnight stasis. The diagnosis in the other cases had been made on the history and x-ray findings, previous hemorrhage and occult bleeding when first studied.

To the above cases of ulcer 2 may be added upon whom gastro-enterostomy was performed before test-meal studies of this kind were instituted. Operation did not result in entire relief of symptoms.

TABLE VI.—Unsuccessful Gastro-enterostomies.

Case.	Free acid.	Total acidity.	Test-meal residue.	Gastric-juice residue.	Ratio.
11	16	32	38	124	1 to 3.2
12	17	35	11	69	1 to 6.0

The consistency of results in repeated observations on some of these ulcer cases is shown by the following figures where cases have been under medical treatment.

TABLE VII.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
2	34	136	1 to 4.0
	49	120	1 to 2.4
	26	162	1 to 6.4

Benefit in subjective symptoms had apparently resulted when the second test meal was taken. An exacerbation of symptoms at the time of the third meal made operation advisable.

TABLE VIII.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
3	55	224	1 to 4.0
	46	187	1 to 4.0
	21	113	1 to 6.0
	52	115	1 to 2.2
	55	137	1 to 2.3
	22	128	1 to 5.0
	41	71	1 to 1.8
	44	105	1 to 2.4
	42	118	1 to 2.7
	51	120	1 to 2.3

This case, under medical treatment, has suffered the usual remissions and exacerbations, refusing radical operative treatment. The test meals have been taken during the last year. For the last four months the patient has been free from symptoms, and during this period the last four meals were examined.

TABLE IX.

Case.	Test-meal residue.	Gastric-juice residue.	Ratio.
4	20	150	1 to 7.5
	22	178	1 to 8.0
	16	99	1 to 6.0
	40	110	1 to 3.0

This case is interesting in that it shows that although there is pyloric stenosis, as shown by large overnight stasis of rice and rasins, the fluid test-meal residue may be small. Operation was refused and the lowering of the secretion ratio followed diet, medication, and systematic lavage. There was marked improvement in subjective symptoms corresponding with the fall of gastric juice secretion.

CONCLUSIONS. The demonstration of an alimentary hypersecretion is strongly suggestive of a chronic gastric ulcer. Whether a low ratio occurs in a case of ulcer of this type must be determined by future observations. How frequently alimentary hypersecretion occurs in conditions other than ulcer cannot be stated on this comparatively small number of studied cases. In a few instances we have found the gastric juice three times the amount of the test-meal residue. A ratio as low as this has proved the exception in those cases in which ulcer has been diagnosticated.

## INTERMITTENT SPINAL CLAUDICATION.

BY FRANK F. D. RECKORD, M.D.,

RESIDENT PHYSICIAN IN THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

INTERMITTENT claudication may be divided into (1) the cerebral type, (2) the peripheral type, (3) the lumbar type, and (4) the spinal type. The arteries most commonly involved are the tibial, brachial, coronary, mesenteric, cerebral, and spinal arteries.

The chief cause is arterial disease, arteriosclerosis, senile calcification, obliterating endarteritis, acute arteritis. Not only are there organic changes in the vessel walls, but also an associated vasomotor neurosis, with a tendency to vascular spasm, which narrows the lumen of the vessels and diminishes the flow of the blood to the parts, with a resulting ischemia. Oppenheim recognized a benign purely functional type due to vascular spasm. Venous changes or diseases may give rise to symptoms of claudication similar to those in case of arterial disease. A secondary change follows in the nerve trunks and fibers as would be expected from impaired nutrition.

The predisposing causes are: (1) Exposure to cold and wet involving the anterior and posterior tibial arteries, (2) use of tobacco (Erb), (3) occupations such as that of marble-cutters who use the pneumatic chisel, and (4) senility. The exciting causes may be grouped under: (1) Syphilis, (2) acute infections, as influenza and acute endocarditis, and (3) alcohol.

It was shown in Charcot's<sup>1</sup> original observations in 1858 that with involvement of the large arteries of the lower extremity, intermittent limping, weakness, painful cramps, and paresthesia may develop in the extremities while walking, disappearing after a period of rest (*paralysie douloureuse intermittente*). The peculiar feature of this is the intermittent character of the symptoms, their appearance only during muscular activity, and their rapid disappearance in the passive state.

Erb,<sup>2</sup> in 1898, showed that more frequently the smaller ramifications of the arterial tree are involved with corresponding changes in the pulsations of the pedal arteries.

Williams<sup>3</sup> has reported a case of intermittent claudication involving an upper extremity. When the condition affects the upper extremities it is accompanied by numbness, the parts being cold, white, and painful, and resembling greatly one stage of the picture presented by Raynaud's disease. By resting and rubbing the hands the symptoms disappear. Frequently those afflicted in this way are obliged to change their occupation.

J. Ramsey Hunt<sup>4</sup> has recently described in a graphic manner the lumbar type of intermittent claudication. In this there is severe pain in the lumbar region, intermittent in character, occurring regularly during activity and ceasing after a short rest. A sufficient amount of blood is supplied during the passive state, which does not suffice, however, for the increased demand of the sacro-lumbar mass during activity, hence the painful cramps and their peculiar intermittent character.

J. Dejerine<sup>5</sup> has described the type of intermittent spinal claudication. He states that the diagnosis from peripheral intermittent claudication depends on the absence of pain and circulatory disturbances and the presence of vesical and rectal symptoms—the condition being one of defective blood supply of the lumbar enlargement. The disorder is more common in males, one side being nearly always affected sooner than the other. The course may be rapid or insidious, but all cases tend to go on to spastic paraplegia if untreated. The organic reflexes are affected from the beginning. The most common symptom being precipitate micturition. The

<sup>1</sup> Compt. Rend. et mém. de la Soc. de Biol., 1858, xii, 225.

<sup>2</sup> Deut. Zeit. f. Nervenheilkunde, 1898, Bd. xiii, S. 1.

<sup>3</sup> Jour. Nervous and Mental Disease, May, 1912, xxxix, No. 5.

<sup>4</sup> AMER. JOUR. MED. SCI., February, 1912, cxliii, 2, 173.

<sup>5</sup> Rev. Neurologique, 1906, No. 8.

Babinski sign is usually if not always present. The ensuing paraplegia may resemble a hemiplegia, as the unequal affection of the two sides is common. The cause of the symptoms must be defective blood supply of the lumbar enlargement, as a result of which only sufficient blood is received for the physiological processes in the passive state, the supply being inadequate for the increased demands during activity. As there have been no cases of intermittent spinal claudication reported in the English language, so far as I know, I feel warranted in presenting these 2 cases:

CASE I.—T. B., aged forty-three years, married, native of Ireland. He was first seen September 10, 1910, and complained of weakness in his left leg and burning sensation and pain in the lumbar region of the back.

History of Present Illness: He noticed weakness in both legs three years ago; this came on suddenly while he was cutting grass. He was told he had sciatica. He continued working, but was compelled to stop from time to time on account of weakness and stiffness in his legs. The condition seemed to be worse in bad weather, and when he did a great deal of walking. He had a burning sensation in his back and at times cramp-like pains.

Past Medical History: He had the usual diseases of childhood, typhoid fever when aged twenty-one years, pneumonia at twenty-two.

Social History: He used alcohol to excess until three years ago. All venereal history is denied.

Family history is negative.

Examination of patient showed the pupils to be equal. Irides responded equally and well to light and accommodation. The knee-jerks were exaggerated. Both legs were spastic, but the left was more so than the right. No clonus was observed. There was slow hyperextension of the great toes when the soles of the feet were stroked (Babinski). No sensory changes were obtainable in any part of the body. Muscular power was somewhat impaired in the left lower extremity. Slight atrophy of the thenar and hyperthenar eminences was observed on the left side. The arm reflexes were all exaggerated, with the possible exception of the right biceps.

The patient came under my observation March 19, 1912. A diagnosis of intermittent spinal claudication having not as yet been made. From him I elicited the following: In January, 1912, he fell and broke his right humerus. Since then his left leg has been weaker and has bothered him considerably. When walking suddenly all power leaves the left leg and he falls unless he immediately receives some support. In a few minutes the power returns and he is able to go on his way. Some of the muscular power leaves his left arm when the leg gives way, and his left foot becomes cold. As the foot becomes warmer his leg feels better. He has good use

of his right leg, but it becomes a little cold at times. On an average of once a day he has attacks in which his left leg jerks, the leg being flexed on the thigh, and is drawn up forcibly. The great toe moves backward and forward. This takes place lying or sitting; but if he gets up and bears some weight on the leg these movements stop. If he bears much weight on it, the leg suddenly gives way and he falls. Sometimes his back also feels weak, especially when the leg gives way. The left foot, when the attacks of weakness occur, feels as though it were swollen, but when examined it is found to be normal. Once in a while his left hand feels clumsy and he is unable to pick up various articles. In a short time this passes away and it feels normal.

After lying down and on awaking in the morning he can urinate with ease; however, during the day when up and around he has to stop and wait until the urine comes, then it dribbles, stops, then starts again, and the flow is fairly good, but he has some trouble in voiding the last few drops. The bowels are constipated. His leg always feels worse before a change in the weather, but after the change takes place it again improves. At times he has considerable itching on the sole of the left foot. At times the left leg and left arm are weak irrespective of each other.

In the physical examination the following facts are prominent: Eyes are normal. Throat is normal. There is no noticeable change in facial muscles and no impairment of sensation in the face. Thorax is normal. Heart and lungs are normal. Abdomen is normal. There is no impairment of sensation.

Dorsal Region: He complains of a sense of weakness in the region of the second lumbar vertebra. There is no impairment of sensation about the genitalia and anus.

Left Upper Extremity: Normal with the exception of numbness, which occurs in attacks daily, radiating from the shoulder to the fingers. Never any pain.

Right Upper Extremity: Negative.

Right Lower Extremity: Patellar reflexes are prompter than normal. In testing for the Babinski there is a slight hyperextension of the great toe when the sole of the foot is stroked.

Left Lower Extremity: There is moderate impairment (changeable in character) of muscular force and power. Muscles are somewhat poorly developed. He has considerable rigidity at times; this is not noticed when the patient has been in the supine position for some time, but is noticed after waking. There is no impairment of tactile, pain, heat, cold, and deep pressure sensations. At times he has the sensation of a drop of water running under the skin and suddenly bursting. There are no apparent tremors. Movements are free in all directions. At times the leg is as if dead, and if the patient desires to cross his knee with this leg, it must be lifted over. Patellar reflexes are exaggerated; this exag-



geration varies and is more striking if tested after walking. The quadriceps extensor group can be seen contracting. He has no ankle clonus. There is a moderate amount of incoördination (heel to knee test). In testing for the Babinski there is a moderate hyperextension of the great toe when the sole of the foot is stroked. He had burning sensations in the left inguinal region two years ago, and not since.

The lower extremities were tested for changes in pain, and thermal sensations after exercise, but there was no impairment.

Gait: The patient holds the left leg as if stiff, and there is very little movement at the knee-joints in walking; the heels scrape on the ground.

Romberg's sign is negative.

Urine and blood examinations are negative.

X-ray examination of the spinal column is negative.

Wassermann reaction is negative.

Blood Pressure: Systolic, 90; diastolic, 50.

CASE II.—J. W., aged forty-seven years, druggist.

His chief complaint is pain in the back, and in walking down steps he has severe pain in the knees. After walking for a few minutes his legs become stiff and powerless, and they drag, so that he must stop for a few minutes and rest, then he can proceed as at first. His present condition began in November, 1911, when he had pain in his back and general weakness. No venereal history is obtainable. He averages one alcoholic drink daily, and uses tobacco moderately.

Physical Examination: Pupils are unequal, the right being larger than the left, and somewhat irregular in shape. They react poorly if at all to light, but react to accommodation. Some slight swaying is present with eyes closed. Gait is spastic in both legs. Reflexes of the upper arm are slightly exaggerated. Power and motion are good. Legs are somewhat below normal in strength. Upon exertion he has violent trembling of his legs. Reflexes are all greatly increased in the lower extremities, but there is no ankle clonus. Doubtful Babinski is present in the left extremity. Some slight hypesthesia in indefinite areas is found in the lower extremities. Dorsalis pedis artery is not palpable on either side. Pulse (radial) is feeble and irregular. Some myocardial insufficiency is observed.

This case was seen in the medical dispensary of the University Hospital.

In conclusion, I desire to extend my thanks to Professor William G. Spiller for his kindly interest in this paper.

## THE METASTASIS OF HYPERNEPHROMA IN THE NERVOUS SYSTEM: JACKSONIAN EPILEPSY CAUSED BY SUCH LESION.<sup>1</sup>

By JOSEPH COLLINS, M.D.,

PHYSICIAN TO THE NEUROLOGICAL INSTITUTE OF NEW YORK,

AND

R. G. ARMOUR, M.D.

CHIEF OF CLINIC TO THE NEUROLOGICAL INSTITUTE OF NEW YORK.

THAT tumors of the adrenals may exist without causing any symptoms is well known, and that metastasis of such tumors may occur in parts of the body remote from the adrenals, without previous or coincident manifestations of disease in the adrenals, is equally well known. The neurologist has small encounter with hypernephroma metastases. Its occurrence in the central nervous system is uncommon. Occasionally, he has to distinguish bone metastasis of it from brachial, pelvic, and other forms of neuralgia, but even this is of rare occurrence.

We have recently had a case of Jacksonian epilepsy, which was found to be dependent upon a metastasis of hypernephroma. The case presents many interesting features, not the least of which is the extraordinary absence of objective signs to indicate the existence of extensive and advanced disease.

The patient was a Bohemian cigarmaker, aged forty-five years, who maintained that aside from an attack of rheumatism, which he had when he was aged forty-one years, he had not been ill since childhood, until he had an attack of unconsciousness four months before he entered the Neurological Institute in July, 1911. The first attack came on suddenly while he was at work, May 9, 1911. He felt a twitching of the left thumb and forefinger, followed by a sensation of numbness and tension, gradually extending up to the shoulder, and then he lost consciousness. Within an hour he felt quite well again, save that he was weak and discouraged. Five hours later he had a second attack, but without loss of consciousness. A few days after this experience he began to have attacks characterized by paresthesia in the left hand and forearm and twitching of the thumb and index finger, which were not accompanied by any disturbance of consciousness, and which were not followed by any loss of dexterity. He had had from one to five such attacks every day for three months following the original attack. The next severe attack that he had was July 13, 1911, he being at that time in the hospital. He had two severe attacks in one day, each lasting about fifteen minutes, and each followed by

a profound sleep. The attacks were typical of Jacksonian epilepsy, the attack beginning as above described and followed by generalized convulsions. A physical examination at this time failed to reveal any signs of organic disease of the brain, nor did the patient complain of any symptoms, save those that have been enumerated. There was no headache, vertigo, disturbance of equilibrium, loss of power in any of the extremities, or disordered function of any of the special senses. He complained only of general weakness, loss of flesh, and of the attacks of twitching or convulsions in the left hand. The attacks were not always the same. At times the sensation in the hand was that of pins and needles, and the twitching might be so slight as to flex only the thumb rhythmically a few times. At other times the sensation in the fingers and hand, wrist, and forearm was of tingling, numbness, tension, and bewilderment, and the motor symptoms were correspondingly greater. The duration of the attacks was from a few seconds to several minutes. He gave up his work because of the frequency of the attacks, and because he felt generally weak. Moreover, the left hand was awkward and weak. He remained in the hospital for one month, during this time he had no major attack, save the one mentioned above.

He reëntered the hospital September 12, 1911. He had by this time developed the only symptom which, aside from the Jacksonian attacks, he ever developed—namely, mild somnolency. He had likewise developed a physical sign which was striking. The left hand, as he lay in bed, assumed a semi-flexed position, with the thumb extended. The hand had the appearance of being atrophied, though no distinct atrophy could be made out; he could move the fingers freely and readily.

Physical examination showed moderate weakness of the left side of the body, upper and lower extremity, and face. The tendon jerks of the left extremities were livelier than those of the right. There was no Babinski phenomenon and no clonus. The abdominal and epigastric reflexes were elicitable on both sides, those on the right side being somewhat livelier than those on the left. There was slight incoördination of the left hand and a distinct impairment of dexterity of this hand. Tactile sensibility, contact sensibility, and pressure sensibility were unimpaired. He did not interpret quickly and correctly postural sensibility in the left hand, forearm, and arm. On several occasions there was distinct astereognosis of the left hand. This symptom, however, was not constant; it would be found one day and not the following day. Wassermann examination of the blood and cerebrospinal fluid was negative. The fluid obtained by lumbar puncture showed no excess of globulin, one cell, and it reduced by Fehling's solution. No abnormality of the thoracic and abdominal viscera could be made out, save that the heart was dilated, its impulse feeble, its sound puerile. The

pupils were circular, equal in size, and reacted promptly to light. The only definite physical sign that existed was an absence of the left plantar reflex.

In the latter part of September an entirely new clinical symptom showed itself in the left hand. This consisted of a rhythmical movement of the thumb and index finger, two or three short adductions of the thumb and index finger, followed by flexor movement only of the index finger and thumb. The first or coarser movements were at the rate of one per second, the slighter at the rate of eight per second. The patient was quite conscious of the movement and experienced considerable discomfort from it. This later manifestation was not accompanied by, or associated with, paresthesia, but since the onset of it the localized convulsions in the hand and forearm became more frequent, sometimes occurring as often as every half-hour. It was also noted that the tendon jerks in the left upper extremity had become much exaggerated since the onset of the rhythmical movement. Although the left hand still had a fair amount of strength and the fingers and hands could be moved, he now complained of a sense of great clumsiness in his hand, and postural sensibility became much impaired. He also complained of severe pain in the back of the hand and wrist; he could not further particularize it. There was no disturbance of contact sensibility or thermal sensibility. The patient had no symptoms of increased intracranial pressure save the somnolency above mentioned. On September 26 it was noted that the rhythmical movement of the thumb and index finger was less in intensity and frequency. At this time the rate was fifty to the minute. On September 25 it was noted that he had three major attacks three hours apart, each of which lasted ninety seconds. The rhythmical movement ceased for one-half hour after each attack. On both of these dates and on September 28 it was recorded in the clinical notes that there was no astereognosis.

Five months after the initial symptom—namely, on October 1, the patient, while lying in bed, had a series of convulsions and died.

To recapitulate: A man, aged forty-five years, who had been in good health developed typical Jacksonian epilepsy, displaying itself by twitching of the left thumb and index finger, paresthesia of the left hand, and forearm and followed on five occasions by loss of consciousness and generalized convulsions. Gradually there developed loss of power and of dexterity in the left upper extremity and to a slight degree in the entire left half of the body. The only definite physical signs were loss of sense of position in the left hand and fingers and absence of the left plantar reflex. There was an inconstant astereognosis of the left hand and a mild increase of the tendon jerks of the left half of the body. A week before his death a slow rhythmical tremor of the left thumb and

index finger, consisting of adductor movements about one per second, developed.

When the abdominal cavity was opened a large whitish tumor was found in the right flank. This tumor had invaded the upper pole of the right kidney, surrounded the adrenal and extended into the under surface of the right lobe of the liver. In various other parts of the liver there were a few metastases up to three-fourths of an inch in diameter. In the wall of the duodenum, near the junction with the jejunum, was a small metastasis one-eighth of an inch in diameter. The only other metastasis found was in the right cerebral hemisphere. This metastasis was one and one-half inches in diameter, situated one-fourth of an inch below the surface midway between the vertex and the base, that is, in the arm area, and more particularly in the hand area.

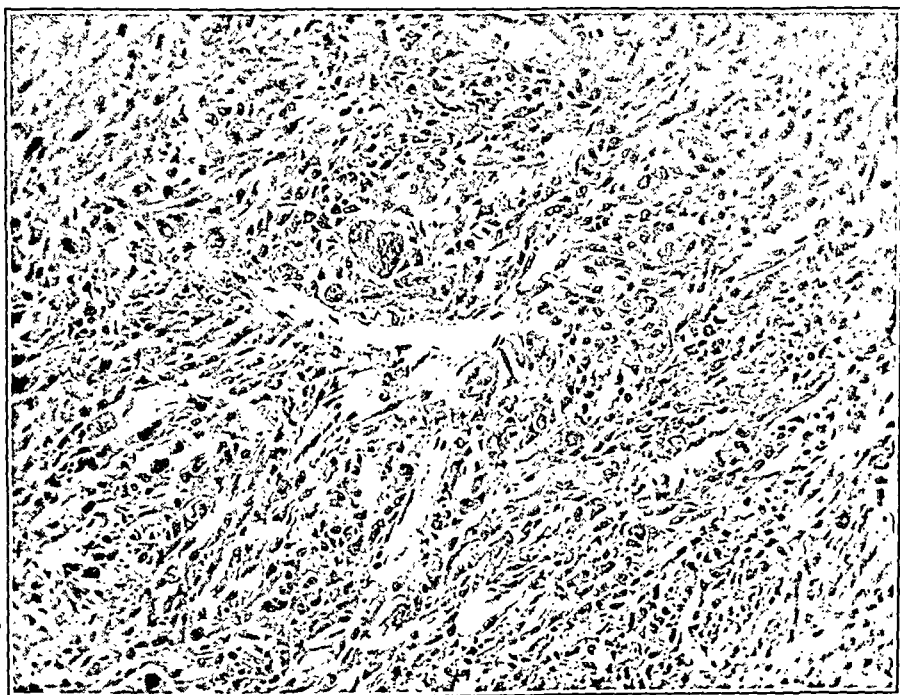


FIG. 1.—Hypernephroma.

Microscopically, the primary tumor mass, as will be seen in the photomicrographs, consisted of cells running in columns arranged about capillaries, the appearance resembling closely that of the cortex of the adrenal gland. The nuclei stain deeply, but the protoplasm stains only lightly with eosin and shows numerous vacuolations. Here and there in the strands are seen some cells much larger in size than the majority, taking a deeper eosin stain and exhibiting granular degeneration or fragmentation of their nuclei (Fig. 1).

In the metastases in the liver the general resemblance to the

adrenal cortex is retained, but is interrupted frequently by indiscriminate masses of cells with no particular arrangement, and by the presence of a greater number of the larger degenerating cells (Fig. 2).



FIG. 2.—Hypernephroma. Metastases in liver.

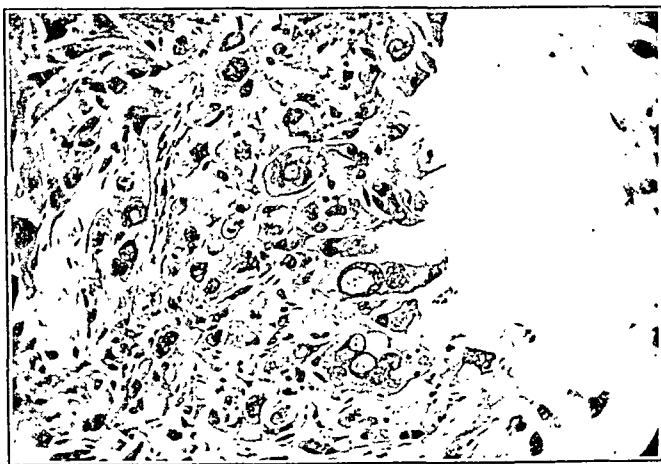


FIG. 3.—Hypernephroma. Metastases in brain.

In the metastasis in the wall of the duodenum the resemblance to adrenal tissue is maintained.

When, however, we come to look at the metastasis in the brain, all suggestion of adrenal tissue is lost. The cells are large in size,

polyhedral in shape, stain deeply, and show nuclei in many stages of degeneration. Some nuclei are small, deeply stained, and show no granulation. Others are large, pale in color, vacuolated, granular, and fragmented (Fig. 3).

Many of the cells in this metastasis have taken on a phagocytic function, and can be seen to have ingested red and white blood cells.

The presence of a tumor of this size in the abdomen, without having given rise to more definite symptoms betraying its presence, seems remarkable.

The abdominal wall was very fat, and though several routine examinations were made, no sign or symptom ever prompted more searching examination.

He had at no time any evidence of hemorrhage into the tumor, such as pain or hematuria, and the only symptom he complained of which is sometimes found with hypernephroma was a frequent aversion to food.

The blood pressure, of course, could be expected to give no information, since the tumor was entirely made up of tissue resembling the cortex of the adrenal gland, and this cortex has never been found to affect the blood pressure in any appreciable manner.

The extraordinary absence of the general symptoms of brain tumor is probably to be explained by the fact that the tumor had not caused considerable increase of intracranial pressure. It was this absence of symptoms that decided us not to submit him to exploratory craniotomy, despite the directness of the localizing sign that existed—namely, the Jacksonian convulsions. The rhythmic tremor that developed shortly before his death is of much interest. It has been generally taught that movements of this character conditioned by intracranial disease are indicated by impulses that arise from, or better said, are coördinated in the thalamus.

Without going deeply into the origin, histology, or dissemination of hypernephroma, we may perhaps say a word or two about this form of tumor. It is one of those which cannot be classed rightly with either the carcinomas or with the sarcomas, and will probably in future be put in a class by itself. It may be benign or malignant; that is, it may exist throughout life confined to its original location and cause no discomfort or menace to the patient's life; or it may be the seat of a hemorrhage, due to its friable composition, and so cause intense pain or even loss of life; or, yet again, it may take on a malignant character and strew the body with metastases.

In its simplest form, as a benign tumor, it can be best studied with regard to its origin. Histologically it consists of strands of cuboid cells arranged in long strands about capillary bloodvessels. This arrangement reminds one forcibly of the appearance of the cortex of the adrenal gland, and this similarity is enhanced by the pres-

ence in the cells of large quantities of a double light refracting fat which characterizes the cells of the cortical adrenal cells. This constituent may be found in the cells of even the most remote metastasis, though in the case which we report it has seemed to have disappeared in the brain metastasis.

In addition to this histological resemblance to the adrenal gland the location of the tumor is also most significant. Besides its occurrence in the adrenal gland itself, where normally we find small adenomas of minute size, hypernephromas occur most commonly in the upper pole of the kidney and in the right lobe of the liver on its under surface. These parts are in very close proximity in the embryo, and when we find metastasis also occurring in the ovaries and testicles, organs which take their origin in the same close proximity, though later descending to their respective sites, we can hardly doubt the origin of this tumor. This conception of hypernephromas must lead one to regard it as a congenital phenomenon. Later in life, sometimes, we see it take on an activity signifying an entire change of character. It starts to grow rapidly, to invade surrounding tissues and organs, and to disseminate metastases in many different parts of the body. The most common place to find these secondary tumors is in bone, but we here record a metastasis in the brain, in which location many statistics regarding hypernephromas record only one or two instances.

---

## METABOLIC OBSERVATIONS ON AMYOTONIA CONGENITA.

BY J. C. GITTINGS, M.D.,

AND

RALPH PEMBERTON, M.S., M.D.,

PHILADELPHIA.

(From the Laboratory of Clinical Chemistry, Presbyterian Hospital, Philadelphia, and the Pepper Laboratory, University of Pennsylvania.)

AMYOTONIA congenita, or myatonia congenita, is a rare condition affecting children, aged up to three or four years, and exceptionally later, with a general proximal pseudoparalysis, for which no satisfactory etiology or pathology has been advanced. According to a recent clinical review of the subject by Haberman,<sup>1</sup> about 35 cases had been reported up to 1910. Since then a case has occurred in the service of Dr. J. P. Crozer Griffith at the University Hospital, Philadelphia, and was reported by him.<sup>2</sup> Griffith has

<sup>1</sup> AMER. JOUR. MED. SCI., 1910, cxxxix, 383.

<sup>2</sup> Archiv f. Kinderheilkunde, 1910, liv, 211; Trans. Amer. Ped. Soc., 1910, xxii, 184.



collected 49 cases, including Haberman's and his own, although he admits that the diagnosis of some of them is doubtful. According to either series, however, the rarity of the disease is evident. Griffith's case, a boy, aged fifteen months, on admission, December, 1910, showed the characteristic findings of amyotonia congenita—extreme muscular weakness without signs of muscular atrophy and without evidence of rickets. The general nutrition appeared to be good. There was absence of the tendon reflexes, and entire absence of contraction both to faradic and galvanic currents.

It occurred to us that some metabolic studies in the case would be of interest. The child's condition during the first few months of his stay in the hospital precluded the possibility of making metabolic observations owing to his extreme asthenia which was increased, from time to time, by slight febrile attacks, the exact cause for which could not be determined. In June, 1911, when he was aged twenty-one months, his condition having improved, we were able, through the courtesy of Dr. Griffith, to obtain a five-day observation. The publication of our findings has been postponed until they could be controlled by similar studies upon normal children of the same age, which we have now made.

In October, 1911, the child developed an attack of bronchitis, quickly followed by pneumonia, which resulted fatally within five days. The autopsy was performed by Dr. B. S. Veeder—the results of which, together with the histological study, were published by Drs. Griffith and Spiller.<sup>3</sup> A summary of their important findings in the muscular and nervous system showed a brain of extraordinarily large size (as large as that of an adult), but otherwise presenting no gross anomaly. The nerve cells of the anterior lobes were scarce, and those present were much atrophied. The anterior roots throughout the cord were smaller than normal, and stained imperfectly by the Weigert-hematoxylin method. A peripheral nerve examined was found to be much degenerated. The intramuscular nerve fibers also showed degeneration. The muscular system (back, forearm, and calf) showed marked atrophy of the fibers in some places; in others the fibers were well preserved. There was an excess of fibrous and fatty connective tissue, increase in size of some muscle fibers, and fatty change within others. The muscle spindles appeared to be normal. From their study of this case and a review of others reported with autopsy, Griffith and Spiller conclude that in the lighter cases of amyotonia the pathological changes may be confined to the muscular tissues. In intense cases the nervous system is affected in a marked degree. The relations of the disease to muscular dystrophy and to the Werdnig-Hoffmann type of muscular atrophy are as yet undetermined. The points of resemblance to both these diseases cannot be ignored.

<sup>3</sup> AMER. JOUR. MED. SCI., 1911, cxlii, 165.

There is grouped under the caption of neurology, however, a considerable variety of diseases, for whose inclusion there little or no etiological or pathological justification can be advanced. Some of these diseases to be sure, do not belong clearly in any other branch of medicine; but in any event they have been largely removed from the consideration of workers in lines outside those of neuropathology, in the broader sense of the word. In the absence of means of attack other than histological study little or no progress has been made toward their solution. Examples of this are well seen in the condition now under discussion, in the muscular dystrophies, paralysis agitans, myasthenia gravis, etc.

In certain previous communications,<sup>4</sup> one of the present writers has endeavored to approach some of these conditions from a different standpoint embodying a "dynamic point of view;" that is to say, a consideration of the body metabolism. The results were interesting and seemed to justify further attempts of the sort when opportunity presented. But few such studies are on record.

There seems to be no adequate reason for the indifference with which these interesting diseases have been regarded in this country by internists and laboratory men at large since the inclusion of such conditions within the realm of neurology is, largely, the result of excursions by neurologists into the field of medicine.

The phenomena of diseases such as those mentioned above are obviously of the widest importance in studying the metabolism of the muscles and of the body as a whole, as is so well exemplified in our recently acquired knowledge of tetany, for instance. But one observation seems to be on record, however, of the metabolic features in amyotonia congenita, and that one is by Spriggs, who studied the uric acid and creatinin and found a low output of the latter in a boy, aged four and one-half years (0.06 gram creatinin *per diem*).

The experiences above referred to in regard to Myasthenia gravis and Myotonia atrophica developed an interesting departure from the normal in the former disease which suggested the advisability of including a consideration of the calcium metabolism in further studies on allied conditions. The case to be reported was therefore, studied with respect to the urinary nitrogen, fecal nitrogen, urinary calcium, fecal calcium, and the creatinin. For control the metabolism of 2 normal children of the same age was also observed. All 3 children were placed upon the same diet and were kept in Bradford frames to facilitate collections. The difficulties incidental to metabolic studies upon young children are too well known to require mention here except to say that they operated to prevent our obtaining an accurate balance in the

<sup>4</sup> Pemberton, AMER. JOUR. MED. SCI., June, 1910; *ibid.*, February, 1911.

case of amyotonia. The essential facts sought for were elicited, however, in regard to the creatinin and fairly clearly indicated in regard to the calcium.

Although an accurate balance was impossible in the case of amyotonia, it was obtained in the 2 control cases as a further index of comparison and for possible future reference.

CASE I.—John, aged thirty-three months; normal; control case.

#### AVERAGE DIET.

Breakfast:	Bread . . . . .	24 grams
	Butter . . . . .	7 grams
	Eggs . . . . .	51 grams
	Milk . . . . .	100 c.c.
Dinner:	Rice . . . . .	43 grams
	Butter . . . . .	7 grams
	Crackers . . . . .	13 grams
	Milk . . . . .	100 c.c.
Supper:	Bread . . . . .	36 grams
	Butter . . . . .	5 grams
	Eggs . . . . .	48 grams
	Milk . . . . .	100 c.c.

#### *Ingesta.*

Nitrogen . . . . .	12.4721 grams
Calcium . . . . .	1.4604 grams

CASE II.—Alvin, aged forty months; normal; control case.

#### AVERAGE DIET.

Breakfast:	Bread . . . . .	36 grams
	Butter . . . . .	10 grams
	Eggs . . . . .	54 grams
	Milk . . . . .	100 c.c.
Dinner:	Rice . . . . .	38 grams
	Bread . . . . .	19 grams
	Butter . . . . .	14 grams
	Milk . . . . .	100 c.c.
Supper:	Rice . . . . .	57 grams
	Crackers . . . . .	13 grams
	Butter . . . . .	10 grams
	Milk . . . . .	100 c.c.

#### *Ingesta.*

Nitrogen . . . . .	11.9805 grams
Calcium . . . . .	1.4248 grams

CASE III.—Charles, aged twenty-one months; amyotonia congenita.

## DIET.

	Nitrogen.	Calcium.
Bread . . . . .	6.8816 grams	0.1594 grams
Rice . . . . .	0.8103 grams	0.0752 grams
Egg . . . . .	4.7388 grams	0.2055 grams
Butter . . . . .	0.1048 grams	0.0372 grams
Crackers . . . . .	0.7548 grams	0.0139 grams
Milk . . . . .	16.4479 grams	3.7652 grams
	<hr/> 29.7382	<hr/> 4.2564

	Before metabolic period.	After metabolic period.	Average.	Kgs.
Weight, Case I, John . .	24.5 oz.	24.14 oz.	24.9 oz.	11.16
Weight, Case II, Alvin . .	24.4 oz.	24.8 oz.	24.6 oz.	11.07
Weight, Case III, Chas. . .	21.8 oz.	22.8 oz.	22.0 lbs.	10.00

## CASE I.—John. April, 1912.

	7th	8th	9th	10th	11th
Quantity of urine . . .	257 c.c.	L	320 c.c.	175 c.c.	155 c.c.
Nitrogen of urine . . .	3.7900 grams	O	4.6592 grams	3.3712 grams	2.4416 grams
Creatinin of urine . . .	0.1041 grams	S	0.1149 grams	0.0547 grams	0.0662 grams
Calcium of urine . . .	Not done	T	0.1168 grams	0.0507 grams	0.0528 grams

Total nitrogen in total feces = 1.7112 grams. Total urinary nitrogen = 10.4720 grams  
 Total calcium in total feces = 1.7054 grams. Total urinary calcium = 0.2203 grams

Total nitrogen egested . . . . . 12.1832 grams  
 Total calcium egested . . . . . 1.9257 grams

Positive nitrogen balance +0.2889 grams. Weighed 24 lbs., 5 oz. before metabolic period  
 Negative calcium balance -0.4653 grams. Weighed 24 lbs., 14 oz. after metabolic period.  
 Daily creatinin average, 0.0786 grams. Creatinin coefficient, 7.04 mg.

## CASE II.—Alvin. April, 1912.

	10th	11th	12th
Quantity of urine . . . . .	154 c.c.	238 c.c.	298 c.c.
Nitrogen of urine . . . . .	2.1905 grams	4.4382 grams	3.1752 grams
Creatinin of urine . . . . .	0.0738 grams	0.1083 grams	0.0850 grams
Calcium of urine . . . . .	0.1615 grams	0.2651 grams	0.1554 grams

Total nitrogen in total feces = 1.4483 grams. Total urinary nitrogen = 9.8039 grams.  
 Total calcium in total feces = 1.2640 grams. Total urinary calcium = 0.5829 grams.

Total nitrogen egested . . . . . 11.2522 grams  
 Total calcium egested . . . . . 1.8469 grams

Positive nitrogen balance . . . . . = +0.7283 grams  
 Negative calcium balance . . . . . = -0.4221 grams  
 Daily creatinin average . . . . . = 0.08903 grams  
 Creatinin coefficient . . . . . = 7.04 mg.

## CASE III.—Charles. June, 1910.

	10th	11th	12th	13th	14th
Quantity of urine	226 c.c.	168 c.c.	213 c.c.	199 c.c.	218 c.c.
Nitrogen of urine	4.627 gms.	3.957 gms. <sup>5</sup>	3.288 gms.	3.7419 gms.	3.864 gms. <sup>7</sup>
Creatinin of urine	0.017 gms.	0.015 gms.	0.018 gms.	Too low to be read <sup>6</sup>	Too low to be read <sup>6</sup>
Calcium of urine	0.07677 gms.	0.02624 gms. <sup>5</sup>	0.0136 gms. No stool today	0.00889 gms.	0.0057 gms. 0.87192 gms. Ammonia nitrogen.
Total nitrogen of feces	. . . . .	2.2862 grams	Total nitrogen of urine	. . . . .	19.478 grams
Total calcium of feces	. . . . .	2.6971 grams	Total calcium of urine	. . . . .	0.1312 grams
Total nitrogen egested	. . . . .				21.7642 grams
Total calcium egested	. . . . .				2.8283 grams
Ingested nitrogen, 29.7382 grams	} gained 1 pound				Positive nitrogen balance
Egested nitrogen 21.7642 grams					
					<u>7.9740 grams</u>
Ingested calcium, 4.2564 grams					Positive calcium balance.
Egested calcium, 2.8283 grams					<u>1.4281 grams</u>
Daily creatinin average	. . . . .				0.0166 grams
Creatinin coefficient	. . . . .				1.66 mg.
Daily creatinin average in Sprigg's case	. . . . .				0.0625 grams
Creatinin coefficient in Sprigg's case	. . . . .				4.0 mg.
Normal, 7 to 11 mg.					

(Creatinin coefficient = the daily creatinin elimination in milligrams of creatinin per kilo of body weight.)

A consideration of the figures reveals some points of interest.

The creatinin shows a great departure in Case III (amyotonia) from both of the normal controls and even from Sprigg's case. The average daily creatinin output, when it could be estimated at all, was 0.0166, whereas in Sprigg's case it was 0.0625, and in our 2 normal cases, 0.0786 and 0.0890 respectively. This gave creatinin coefficients as follows:

Amyotonia congenita (Case III)	. . . . .	=0.66 m. creatinin
Amyotonia congenita (Sprigg's case)	. . . . .	=4.0 m. creatinin
Normal child, Case I	. . . . .	=7.04 m. creatinin
Normal child, Case II	. . . . .	=8.04 m. creatinin

<sup>5</sup> These figures are missing and are averaged from those preceding and following. Some urine was spilled by an attendant, leaving enough for creatinin only, though the total quantity was known from the ward record. Having all the calcium figures but those for one day, it is possible to approximate a balance, since the urinary calcium is low in any event. The nitrogen balance can be approximated in the same way, though with greater possible error.

<sup>6</sup> No reading possible with 10, 20, or even 40 c.c. urine. This was corroborated by Dr. Wm. Welker.

<sup>7</sup> On this day the nitrogen of the ammonia was approximately 22.3 per cent. of the total nitrogen.

Until we know the full meaning of the creatinin excretion, interpretation of such results must be guarded, but they would seem to be valuable, at least from the diagnostic standpoint, in differentiating amyotonia from the many conditions with which it may be confused, especially if the involvement be slight. To what extent these figures, together with Sprigg's, indicate a true disturbance of the internal muscular metabolism, is problematical but they are certainly highly suggestive.

As mentioned before, an exact calcium balance was impossible in our case, though in any event the inequalities in the excretion of calcium necessitate guarded conclusions as to its elimination, unless the metabolic period be protracted or the differences observed great. The development of fever after the last metabolic day recorded, prevented the continuation of our observations and subsequently the condition of the child, never very robust, precluded a repetition of the experiment. So far as our figures go, however, and the general facts seem fairly clearly indicated, there is no evidence of marked disturbance in the calcium metabolism.

In observations on a case of myasthenia, previously mentioned, a decided calcium loss was noted over a metabolic period of a week, and it was thought that the present case might show some analogy to it; the opposite is suggested, however.

In conclusion, obligation should be expressed to the Board of Managers of the Presbyterian Hospital, Philadelphia, for the installation of the facilities which have made this and other studies possible. Acknowledgment is also due Dr. Damon B. Pfeiffer, director of the pathological laboratory, for his courteous coöperation on many occasions.

## REVIEWS

---

A MANUAL OF SURGICAL TREATMENT. By SIR W. WATSON CHEYNE BART., C.B., D. Sc., LL.D., F.R.C.S., F.R.S., Hon. Surgeon in Ordinary to H. M. the King, Senior Surgeon to King's College Hospital; and F. F. BURGHARD, M.S. (Lond.), F.R.C.S., Surgeon to King's College Hospital, and Senior Surgeon to The Children's Hospital, Paddington Green. New edition entirely revised and largely rewritten with the assistance of T. P. LEGG, M.S. (Lond.), F.R.C.S., Surgeon to the Royal Free Hospital; and ARTHUR EDMUNDS, M.S. (Lond.), F.R.C.S., Surgeon to the Great Northern Central Hospital, and Surgeon to Out-Patients, The Children's Hospital, Paddington Green. In five volumes. Vol. I, pp. 552; 223 illustrations. Vol. II, pp. 570; 252 illustrations. Philadelphia and New York: Lea and Febiger, 1912.

THE first edition of this Manual of Surgical Treatment comprised seven volumes and was published from 1899 to 1903. The present edition is being issued in five volumes. The work has been entirely revised and largely rewritten; for this purpose the authors have invoked the assistance of Messrs. Legg and Edmunds, because, as the preface informs us, "the pressure of other work rendered it impossible for the original authors to undertake a task of such magnitude with any hope of being able to complete it within a reasonable time." The authors have also enlisted the advice and assistance of Dr. Silk, Dr. D'Este Emery, Dr. Arthur Whitfield, and Mr. A. D. Reid, who have supplied material for the sections dealing with such special subjects as anesthetics, blood examinations, preparation and use of vaccines, etc.

The design of the work is to afford the reader clear and practical advice on the treatment of all conditions in surgery. Pathology and diagnosis are not entirely ignored, but are discussed only when absolutely necessary to explain the treatment advocated. The methods of treatment recommended are such as have proved acceptable to the authors, and in very few instances is it apparent that they have not been employed and tested personally. These features are those which constitute the work a Manual in the intellectual sense. There are few references of historical or bibliographical interest; contemporaneous writers seldom are quoted by name, even if their practices are adopted; and the teaching

inculcated rests in almost all instances on the unsupported *ipse dixit* of the distinguished authors. This is as it should be for a work of this kind, which is neither a text-book, a monograph, nor an encyclopædia. It is a Manual. And in the true original sense of the word the work is a manual also. Each volume is handy in size, in spite of the fact that each contains much more matter than one volume of the previous editions. It is a work for constant use.

In the first volume what is now popularly spoken of as general surgery, and which formerly was described as the principles or the institutes of surgery, is discussed in some three hundred pages; the subject of deformities is also included (about 150 pages); and an appendix is added in which Dr. Silk discusses anesthetics, and Dr. Emery describes in rather summary fashion methods of blood examination, the preparation and use of vaccines, etc.

Of course, going through the chapters page by page, much is found worthy of comment. Not all of these points can be discussed here. A few omissions may be noted: No mention of position in the control of hemorrhage; nothing about continuous baths in the treatment of burns; nothing about carbolic acid injections in tetanus, and the advice, which we regard as a fault of commission, to administer intracerebral injections of antitoxin in this disease. Direct transfusion of blood is ignored. The spelling "Scepticæmia," which occurs repeatedly in the table of contents, should not have escaped the proof-reader's eye.

Antisepsis still is preferred to asepsis, and the chapters on wound treatment are one of the portions of the work which seem in the opinion of the authors to have required least revision.

The statement that the decision for or against a mutilating operation for malignant growth should be left to the patient, is one that brings up anew the moral duty of surgeons. No doubt in all cases the ultimate decision for or against operation rests and must rest with the patient or his friends, for the tumor belongs to the patient and not to the surgeon. But surely the surgeon should not be regarded, much less should he regard himself as a mere machine, to do the cutting if the patient so decides, or to stand by in idleness if the patient declines. We believe the surgeon in such cases should be more than a passive onlooker. Every patient knows that after a serious operation he may die or he may get well, and that the degree of mutilation may be extreme if he survives. But what he looks to the surgeon for in his dire extremity, is not a statement of the percentage mortality of the proposed operation, but the expression of a sincere conviction that in this individual case the operation is or is not advisable. This is what a good surgeon can tell far better than even the most intelligent patient; and when even the most timorous patient feels that the surgeon stands between him and grim fate in such an attitude as



this, there are very few instances in which this throwing the entire responsibility on the surgeon is not a consolation to the patient and all his anxious family. Hence we believe the statement of the authors, that the surgeon should content himself with placing the facts fully before the patient, is an error.

The chapters on deformities are scarcely equal to other portions of the book. Nearly seven pages are devoted to so simple a thing as tenotomy of the tendo Achillis and the after-treatment, and much of this is quite unnecessary twaddle. The treatment of congenital dislocation of the hips and of scoliosis is such as was employed nearly ten years ago; these sections should be entirely rewritten.

Dr. Silk, in his discussion of anesthetics, shows the usual modern tendency away from the use of chloroform.

Dr. Emery says of the von Pirquet test for diagnosis, that it is "almost absolutely trustworthy in children up to the age of twelve or fourteen years;" of the subcutaneous test, for older patients, he gives 0.001 gram first, and if no reaction occurs, goes at once to 0.003 or 0.004 gram. Treatment with tuberculin he considers only a *pis aller*; it is difficult to cure by it lesions in which there is a large amount of caseous material or much fibrosis; "good results," he adds, "are occasionally obtained with tuberculous glands, but this is the exception, and as a rule it is better to remove them."

The second volume includes treatment of lesions of the skin and subcutaneous tissues, nails, lymphatic vessels, and glands, fasciæ, bursæ, muscles, tendons and their sheaths, nerves, veins, arteries and aneurysms; as well as bones, in which latter section are comprised fractures, bone diseases, rickets, and tumors of bone. The volume closes with two chapters on amputations.

Expert advice has been enlisted from Dr. Whitfield on the treatment of lupus, and from Mr. Reid on the treatment of rodent ulcer by radium and the *x*-rays.

The authors strangely cling to the fearsomeness of pre-antiseptic days in their timidity about opening a chancroidal bubo. Modern surgery has demonstrated that secondary infection is the only thing to be feared; and pathologists seem to believe that the bacillus of Ducrey is self-destroyed by the pus which it produces.

As regards the treatment of aneurysms, the authors show, with continental surgeons, a preference for extirpation of the sac over the method of Matas. This they damn with faint praise as follows: "We have given the full details of this operation because it has been done already with a fair amount of success in a considerable number of cases, especially in America. It must be, however, difficult to perform successfully, and it is probable that further experience will show it to be only of limited applicability." Many new illustrations have been introduced in the chapters on ligations,

and in most other respects these sections have been brought fully up to date; there is no mention, however, of the posterior route for ligation of the first part of the left subclavian artery.

Fractures are considered at great length, nearly 200 pages. The authors favor the administration of a general anesthetic for reduction in almost all cases; they favor operation "as soon as possible" when it is called for, and they think it is called for rather frequently. They do not except from this rule children, in whom it is well known that even wide separation of fragments may give no disability or shortening if alignment is preserved; and they do not recognize that oblique require less accurate reduction than transverse fractures. There is no mention of nail extension after the methods of Codivilla and Steinmann, nor the use of a compound pulley for reduction, or of the possibility of reduction by angulation. They approve massage and mobilization in moderation. In cases of compound fractures they urge extensive operation with plating or use of wire fixation.

Volkman's contracture is discussed as a complication of fractures; but strangely there is no mention whatever of Jones's very efficient orthopedic treatment of this condition. Apart from operation they mention only massage and passive movements under the heading of non-operative treatment.

Their practise of beginning passive movement in the case of elbow fractures at the end of a fortnight and their insistence that *full* extension, flexion, supination, and pronation must be enforced once daily from that time on, explain their further statements that not only do adhesions occur in the joint, but a considerable mass of callus is thrown out, etc. If, after accurately reducing the fracture, and keeping it reduced for about three weeks, they would then leave the child's elbow alone, they would be surprised to find that recovery of full function would occur without any callus or the necessity for any passive movements.

The sections on osteomyelitis are not up to date; thorough scraping out of the medulla in acute cases is still recommended, though it was shown by Nichols, a number of years ago, to be not only unnecessary but harmful. The paragraphs on bone transplantation read like ancient history, since the recent work in this line of J. B. Murphy, but as the present volume antedates the publication of these remarkable successes, the authors are not to blame.

Little change is apparent in the chapters on amputations; though the authors bravely commence the subject by pointing out the greater deliberation of present-day operating and the increasing favor of irregular flaps, they at once revert to the description of stereotyped forms. Nor is this to be condemned, because the types must first be learned, and learned well, before a surgeon can successfully introduce variations of his own. But surely in a

work of this size there should be space for a description of Bunge's aperiosteal method for the purpose of securing end-bearing stumps, as well as some mention of amputations for cinematic prosthesis.

The volumes, as already noted, are of convenient size; the paper is good; the type is clear and of fair size; and very many new illustrations (mostly half-tones) have been added, the old ones being discarded where something better was available. There is, however, a tendency toward repeating the same illustration an unnecessary number of times. But the work fulfils its purpose, and will be heartily welcomed by the profession. A. P. C. A.

---

PELLAGRA, AN AMERICAN PROBLEM. By GEORGE M. NILES, M.D., Professor of Gastro-enterology and Therapeutics, Atlanta School of Medicine. Pp. 253. Illustrated. Philadelphia and London: W. B. Saunders Co., 1912.

PELLAGRA has been under observation and study in European countries for nearly two centuries, and yet little accurate knowledge exists as to its etiology, transmission, or treatment. It has at last come into our own country and is presenting its problems to us in a very definite form. The scourge, for such it promises to be unless active measures are at once instituted to check it, is so frightful and awful in its results that any work or observation which promises to clear up its mysteries should be gladly welcomed. In the present work Niles has done us a great service in presenting in brief form the present ideas of pellagra as culled from the writings of many observers abroad and in this country, as well as from his own rather large experience in the study and handling of this disease.

The work is divided into ten chapters. The historical sketch and the chapter on etiology are particularly interesting, and bring out strongly the relationship between pellagra and spoiled maize. And although this etiological relationship is not generally accepted, the author feels that he is justified in closing the chapter on etiology with a reiteration of Lombroso's theory that "In pellegra we are dealing with an intoxication produced by poisons developed in spoiled corn through the action of certain microorganisms in themselves harmless to man."

The chapter on symptomatology and course is well systematized and frequently interspersed with clinical illustrations and case reports to show the many and varied manifestations of the disease.

The chapters on treatment and prophylaxis cover well the present ideas on these subjects, but they must both be necessarily a little vague until the question of etiology is definitely settled.

An interesting and instructive portion of the book is the chapter on animal experimentation and deductions in which the author brings his work up to the knowledge of the day from the experimental side.

There seems to be no great advance in our knowledge of the disease described nor any radical or new ideas expressed, but the work stands as a very complete *resume* of the best and most recent conceptions of the disease, and a starting point for the advance work of the future which must come before complete solution of this "American problem" can be reached. The book is well put together, is very readable, well printed, and the illustrations are unusually good.

F. H. K.

---

CLINICAL DISORDERS OF THE HEART BEAT. By THOMAS LEWIS, M.D., D.Sc., M.R.C.P., Lecturer in Cardiac Pathology, University College Hospital Medical School. Pp. 104, 48 diagrams. London: Shaw and Sons; New York: Paul B. Hoeber, 1912.

THERE are few who are not aware of the great strides that have been made in recent years regarding our knowledge of the mechanism of the heart beat and its disorders, by means of precise graphic methods. Because of the difficulty of applying these methods without special training and study, disorders of the heart beat have not received from the majority of medical men the attention that their importance merits. Many are still content to speak of a pulse rhythm in vague terms such as "very irregular" or "somewhat irregular" or "intermittent" or "bigeminal," without attempting to identify these disturbances exactly, as they can and should be.

It has long been noted that only in certain cardiac cases, digitalis preparations have been efficient in lowering the pulse rate and improving the patient's condition. Where it has not been efficient, the preparation has been blamed and another form used, or one of the other remedies with more or less reputation as a cardiac "stimulant" has been substituted. We know now, thanks mainly to the careful observations of James Mackenzie, that the nature of the disturbance determines the efficacy of the drug; that the totally irregular pulse of auricular fibrillation is *par excellence* the condition responding most frequently to medication by drugs of the digitalis group; that hearts with normal rhythm respond in not more than 30 per cent. of cases; and that various other types of irregularity either do not call for the drug or even contraindicate its use. It, therefore, behooves the medical attendant to recognize very clearly beforehand what the results of his medication are

likely to be. This he can do by simple means without graphic records; and it is to help in such recognition that Lewis has written this hand-book. How well he has done it, any one acquainted with his previous writings and his numerous contributions to the field of cardiac research will know.

The book comprises seven chapters on sinus irregularities, heart-block, premature contractions (extrasystoles), paroxysmal tachycardia, auricular fibrillation, and pulse alternation. In each instance, the nature of the disturbance, its etiological and pathological relations, its subjective symptoms, recognition, prognosis, and treatment are described. Most cases of pulse alternation can scarcely be recognized without graphic means, and here Lewis recommends the use of a simple instrument, such as the Dudgeon sphygmograph. The arrangement of the book is methodical, and its style as clear and concise as the book itself is brief. Lewis aims to bring to general recognition essential facts that have hitherto been known to comparatively few. His book is a valuable contribution, and deserves to be widely read. H. G. S.

---

DELAYED AND COMPLICATED LABOR. By ROBERT JARDINE, Professor of Midwifery in St. Mungo's College, Glasgow. Pp. 343; 107 illustrations, 3 in colors. New York: William Wood & Co., 1912.

THIS book is evidently designed, on the principle of clinical lectures, for ready reference and to assist in a rapid decision as to plan of treatment in all the emergencies likely to be met in obstetric practice. As such it will prove useful. Many points about it are exceedingly good, notably the chapters on hemorrhage; the routine and operative treatment of eclampsia; the chapter on forceps operations and embryotomy, and especially the pages (Chapter X) on Baudl's contraction ring. This latter subject is fully and ably treated, whereas in many similar books it is passed over in a most superficial manner, although it would be difficult to imagine a complication that would get a man of moderate experience into deeper water in so short a time as a case of retraction ring improperly managed. The author states that this is a "one man book," and that he hopes it will be so considered. There are many points, of course, where the technique described is open to discussion and perfectly justifiable difference of opinion, but there can hardly be two opinions as to the aseptic technique, which is distinctly bad. Rubber gloves, universally, do not seem to be known in Glasgow, and hardly an illustration of technique but shows bare hands and arms. Again, many of the illustrations are

not good, especially for the use of medical students, for whom clearness is an absolute essential. Again, the almost veterinary Champêtier bag will not reap much favor here, where it has been almost discarded. There is no mention of blood pressure in the otherwise excellent article on eclampsia; or of Brunn's extra-peritoneal Cesarean section, at least as important an operation as the Porro. In future editions, the chapter on pelvic deformities could be improved, for use in this country, by the inclusion of measurements in centimeters as well as inches.

The arrangement of the book is good, however, with the headings in heavy type and well adapted to quickly finding the information sought, and the work should prove of value in the field it covers.

J. C. H.

---

#### SURGERY OF DEFORMITIES OF THE FACE, INCLUDING CLEFT PALATE.

By JOHN B. ROBERTS, A.M., M.D., Professor of Surgery in the Philadelphia Polyclinic; Surgeon to the Methodist Hospital, Philadelphia, etc. Pp. 273; 273 illustrations. New York: William Wood and Co., 1912.

THIS work gives a detailed account of the congenital and acquired deformities of the face, with their correction by surgical means, profusely illustrated with cases from the wide personal experience of the author. His special leaning to plastic surgery has made him an authority on the subject.

The chapters on hare-lip and cleft palate are probably the most important in the book, and are unsurpassed for clearness in the description of methods of treatment. The author shares the opinion of Lane and Brophy that congenital cleft palate should be closed as early in life as possible, and that it should be operated upon first in cases combined with hare-lip. The operative methods of Lane are especially advocated for cleft palate, and are fully described and illustrated.

There is a useful chapter on skin diseases requiring surgical treatment. Three modern methods of treatment of skin lesions are not described, viz., vaccine therapy in acne vulgaris, desiccation of small growths such as warts, moles, and epitheliomas, with the high frequency current, and the employment of carbon dioxide snow for the obliteration of nevi and other growths. As these procedures have all met with recognized success, it is to be regretted that they are not at least mentioned.

Dr. Roberts' views on the treatment of hypertrophied tonsils do not agree with those of laryngologists at the present time. In advocating removal only of the portion of the organ projecting into the fauces, he apparently overlooks the fact that it is the

"buried" variety—which does not project at all—that is most frequently diseased, and therefore requires complete extirpation.

The author probably recognizes as well as anyone the difficulty of making complete a regional work of this kind without infringing on the fields of specialists in ophthalmic and rhinologic surgery. No doubt this is the reason he has described at length such conditions as ectropion, ptosis, symblepharon, etc.

The text is profusely illustrated with excellent cuts, most of them original. Fig. 95, taken from Bryant and Buck's "Surgery," does not show the correct anatomical relation of the tongue and palate with the mouth closed. The dorsum of the tongue should be in close contact with the roof of the mouth and soft palate, and the space between it and the post-pharyngeal wall should be much narrower. There are a few typographical errors of minor importance.

Frequent references to the literature, clearness of expression, and attention to detail, combine to render the book the most complete and useful of modern works on the subject. R. H. I.

DIE STÖRUNGEN DES FARBENSINNES IHRE KLINISCHE BEDEUTUNG UND IHRE DIAGNOSE. VON DR. HANS KÖLLNER, Privatdozent an der Universität Berlin, Assistent der Universitäts-Augenklinik. Pp. 415; 33 illustrations and 3 colored plates. Berlin: S. Karger, 1912.

HERE is a book of 415 solidly printed octavo pages devoted exclusively to disturbances of the color sense. A work of this size upon such a limited subject allows of ample opportunity for a thorough exposition and discussion of every factor, theoretical and practical, which can enter into the subject matter. Indeed, while the author and the profession are both to be congratulated upon the former having brought together about all that relates to the matter in hand, the reader may entertain the thought that there is almost too much and that condensation would have spared him some hours of rather weary labor; for the book is by no means easy reading, partly owing to the nature of the subject which trenches upon psychology, physiology, and physics, with all of which sciences the reader should have some acquaintance. Following a short discussion of the normal color sense, which is the one portion of the subject we might wish that the author had treated somewhat more *in extenso*, the congenital anomalies (monochromatism and dichromatism) and incompleteness of normal trichromatism are taken up.

Among the callings unfavorably influenced by defect of the color

sense, railway and marine service, art, the author gives a place to that of the practicing physician; defects in whose color sense will interfere with the ready recognition of certain exanthemata of the skin and mucous membrane, commencing icterus, color changes in the eye ground, etc., as well as certain appearance in chemical tests and microscopic diagnoses, for example, the methyl-violet test for gastric juice, staining effects upon bacteria, etc.

Of acquired disturbances of the color sense, which occupy the remaining three-quarters of the work, the various forms are discussed *seriatim*, blue-yellow blindness, progressive red blindness, total color blindness together with the various forms of chromatopsia and cortical disturbances. Pathological changes in the dioptric apparatus, diseases of the retina and choroid, and of the optic nerves and tracts are considered in detail as affecting the color sense. The neuroses, hysteria, neurasthenia, etc., are given a chapter to themselves.

The average reader whose acquaintance with disturbances of the color sense has been derived from the meagre accounts with which even the best of the text-books content themselves, will experience surprise at the extent of the subject and its numerous subdivisions. The simple tests with the Holmgren yarns and the usual methods of investigating the color sense in railway employees are very elementary and fail in many changes to uncover important defects, to say nothing of establishing an exact diagnosis. The careful investigations which have been made in the last decennial have had to be sought for in the periodical literature where they have been widely scattered and often inaccessible. This is the first attempt to bring the results together in a single volume.

T. B. S.

---

DISEASES OF INFANTS AND CHILDREN. By HENRY KNIGHT CHAPIN, Professor of Diseases of Children, New York Post-Graduate School and Hospital, and GODFREY RÔGER PISEK, Professor of Diseases of Children, University of Vermont. Second edition; pp. 617; 181 illustrations and 11 colored plates. New York: William Wood & Co..

THE second edition of this book appears with but slight changes in the text. The additions are such as would be expected, and include virtually all the recent advances in medical sciences pertaining to pediatrics. The authors have only added 27 pages and 2 illustrations to the new edition, thus preserving the compact and convenient size of the volume. The chapter on special examinations might well have been entirely omitted, or at least considerably abbreviated. This applies particularly to the paragraphs



on the Wassermann test, dealing with the theory of the reaction. This space, some 6 pages, could have been more advantageously employed in elaborating throughout the book the too brief pathology of the various diseases rather than going into an elaborate discussion of a subject more or less foreign to a work of this kind. In the same way the various tuberculin reactions, the Widal test, and such diagnostic methods might better have been abbreviated and then incorporated under the specific diseases with which they are associated.

The chapters on infant feeding and the acute exanthemata are particularly valuable. The author handles the subject of infant feeding in a simple and elementary manner which is of great advantage not only to the medical student for whom the work is particularly intended, but also to those other readers of pediatric text-books, the young mothers. The subject is dealt with from a physiological standpoint, and the reader thus obtains a clear conception of infant feeding before advancing to the more intricate problems of the subject. The authors favor the top milk method of modifying cow's milk, the most convenient and satisfactory method yet devised for properly modifying the milk.

The exanthemata are taken up carefully and the rashes described fully and in detail. The value of this chapter is much enhanced by the addition of five colored plates illustrating the various rashes, thus firmly fixing upon the student's mind the general characteristics of these rashes in a way impossible by a mere detailed description of conditions which must be seen to be remembered.

The chapters on the commoner surgical diseases, the commoner diseases of the eye and the ear, and the diseases of the skin, while necessarily brief, are particularly of value not only to the student, but to the general practitioner, who is often at a loss to know where to turn for advice about the diagnosis and treatment of these conditions in children.

This edition preserves the same satisfactory typography and illustrations as are found in the first edition. With the careful changes and additions that have been made, the authors can safely be assured that this new edition will receive the same satisfactory welcome by students and practitioners as the earlier volume.

J. H. M., JR.

---

PREVENTABLE CANCER. By ROLLO RUSSELL. Pp. 164. London: Longmans, Green & Co., 1912.

THE gropings for the cause of cancer have led in many directions. In this book statistics have been industriously compiled and arguments advanced in support of the thesis that cancer is a

disease that is due largely if not chiefly to faulty habits of eating and drinking that come in the wake of civilization. Reduced to its simplest terms the argument is as follows: Cancer is due to some form of irritation as is seen in "pipe" and "chimney-sweep" cancer. The races and communities which are most scourged by cancer are those that eat and consume stimulating drinks to excess. Therefore, it is probable that these indiscreet habits are the irritant factors at the bottom of the prevalence of cancer. There is much in the book to interest the student of cancer, but after perusal the reader will probably agree that the inductive hazard is too great to compel agreement with the author's convictions. D. B. P.

---

GONOCOCCUS INFECTIONS. By MAJOR C. E. POLLOCK and MAJOR L. W. HARRISON. Pp. 218. London: Oxford University Press, 1912.

For student and practitioner for whom this book is designed, it may be recommended as a clear and altogether excellent summary of our knowledge of gonococcus infections. The treatment in its concise and practical detail bears evidence to the experience of the authors and possesses the advantage of not being encumbered by a multiplicity of recommendations drawn from the literature. Vaccines are highly recommended in the treatment of the metastatic infections. D. B. P.

---

AIDS TO HISTOLOGY. By ALEXANDER GOODALL, Lecturer on Physiology, School of Medicine of the Royal Colleges, Edinburgh. Pp. 135; 20 illustrations. New York: Wm. Wood & Co., 1912.

THIS is an attempt to present the essential facts of histology in a simple manner, and in small compass for the junior student. The author has a direct, succinct style and makes the most of the short space he has allowed himself. The list of organs considered is complete, and in general the statements are trustworthy, although all may not agree with his description of cardiac muscle. It is often obvious that the clearness of the descriptions suffers from too much condensation. W. H. F. A.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**On the Causation of Parenchymatous Nephritis.**—GEORGE W. WATSON (*Brit. Med. Jour.*, 1912, i, 822) reports that beyond the association of acute nephritis with the acute fevers, little is known regarding its etiology. Our knowledge is even more vague in regard to the causation of chronic nephritis. To obtain some further insight into the etiology of renal inflammations, Watson has analyzed 100 cases of nephritis in the wards of the General Infirmary at Leeds, excluding cases of interstitial nephritis, or primary sclerotic kidney occurring beyond the middle period of life. Of this series, 80 were undoubted chronic kidneys of either the "large white," or "small white indurated" type. Watson has considered these together as chronic parenchymatous nephritis. It appears that the period of life in which the onset of symptoms is commonest is between twenty and thirty. Acute infections have little or nothing to do with the production of the disease. The effect of long continued sepsis is not clear. Several patients gave a history of uniform good health except for frequently recurring "sore throats." It is therefore not unlikely that absorption of products from organisms may occur without indication of infection. Chronic lead intoxication is well recognized as a potent factor. In only 3 of Watson's cases was it possibly significant. There is no evidence that alcohol was of importance. The only definite effect appeared to be the determination of symptoms in an already existing nephritis. Watson believes that none of the factors enumerated act more than as contributing causes, and that symptoms in an adult whether suggesting an acute or chronic nephritis indicate in the majority of cases a chronic renal change. Of the fundamental cause practically nothing is known. Watson has

considered in this analysis as genuine acute nephritis, those cases in which albumin and casts disappeared permanently with the symptoms after a short time. There were 18 such with diagnosis confirmed in one. All but 2 occurred under thirty, bearing out the commonly accepted view of age incidence. There was no single convincing instance of primary acute nephritis arising from cold. Watson regards this rather as a factor producing the onset of symptoms in an already existing chronic disease, contributing by depressing the general health, and thus favoring the operation of the true cause. On the whole, Watson thinks that acute nephritis is not a common disease, and is usually due to the direct effect of some infection. The majority of cases recover completely. The diagnosis can seldom be made with certainty during the acute attack, and therefore prognosis cannot be safely given, until after at least a few weeks' interval.

---

**On the Function of the Circle of Willis.**—S. P. KRAMER (*Jour. Exper. Med.*, 1912, xv, 348) reports that in 1664 Dr. Thomas Willis published "Cerebri Anatome." Since then it has been generally believed that the circle of Willis was a kind of reservoir from which the different parts of the brain drew their blood supply. Kramer experimented with 50 live dogs and 3 monkeys in the following way. The animals were anesthetized and injected in a carotid or vertebral artery with a solution of methylene blue. The circulation was not interfered with. The animals were killed by opening the heart two minutes later. The brain and cord were removed and the distribution of dye noted. The results obtained by this method showed constant results. Kramer found that a carotid injection distributed methylene blue to the areas supplied by the anterior and middle cerebral, anterior choroid, and posterior communicating arteries on the same side. If a vertebral artery was injected with the others unobstructed, the stain went to the areas supplied by both vertebral arteries, the basilar, and both posterior cerebrals and their branches. If one vertebral artery was tied and the other injected, the staining was incomplete on the tied side. If one carotid was tied and the other injected, the parts were stained normally. But if both carotids or both vertebrals were tied, and one of the other vessels injected, the separation of areas disappeared and the stain was carried forward or backward as the case might be. In other words, the circle of Willis is an antero-posterior anastomosis between the carotid and vertebral vessels, which under physiological conditions does not permit the mingling of blood streams. When, however, either the anterior or posterior branches are completely blocked, the anastomosis will supply blood. These observations were controlled pharmacologically by injecting into the vertebral artery "bulbar poisons" which ought to produce on the centres in the medulla results which they would not cause if injected into the carotid. Alcohol, ether, and chloroform were used, both alone and in defibrinated blood from the same animal to rule out the possibility of emboli. Blood pressure and respiration were recorded. The results obtained entirely confirmed Kramer's previous observations.

---

**Experimental Studies on the Administration of Salvarsan by Mouth to Animals and Man.**—To determine the primary effects of salvarsan by mouth, JOHN A. KOLMER and JAY FRANK SCHAMBERG (*Jour. Exper.*

*Med.*, 1912, xv, 498) administered it to a series of cats, rabbits, and dogs, in pills, capsules, or dissolved in milk and water. Results showed that the drug was without immediate toxic effects, when given in this way, to animals, in a relatively large single, or in multiple smaller doses. No late or secondary poisonous effects attributable to arsenic were seen. In doses equivalent to those used in man, no appreciable degenerative changes were found in the principal organs, within ninety-six hours. Kolmer and Schamberg consider the question of absorption of salvarsan from the intestines worthy of further study. Experiments were made with gastric contents, feces, bile, and urine which demonstrated that within twenty-four hours of ingestion of salvarsan, arsenic may be found in both bile and urine. It is probable that only a portion is absorbed, and this quickly eliminated. When the drug is given, by the mouth to cats, the number of bacteria in the intestinal tract appears to be reduced, most strikingly in the lower end of the ileum. Finally, salvarsan was given by mouth in capsules containing 0.100 to 0.600 grams to 7 syphilitic patients. One within four weeks received 2.4 grams without toxic effect. No symptoms of arsenical poisoning were encountered, unless vomiting and diarrhea, which did not occur in all cases, be considered such. Thus given, the drug exerted a therapeutic influence, but too feeble, Kolmer and Schamberg believe, to warrant its use by this route.

---

**"Floating" or Movable Kidney Considered from the Practitioner's Standpoint.**—SIR MAURICE ABBOT ANDERSON (*Practitioner*, 1912, lxxxviii, 625) believes that the two chief causes which give rise to symptoms from a movable kidney are the associated sagging of other organs, and the liability of a freely movable kidney to permit the ureter to become bent on itself. Thus symptoms are referred to the nervous system, reflexly, and the digestive or genito-urinary systems. Very often the condition may exist without any trouble save a dragging pain in the side, and tenderness of the kidney when found and manipulated. The nervous and digestive symptoms result, as a rule, from "dropped stomach" producing intolerant dyspepsia. Such cases, Abbot Anderson asserts, invariably get well provided means are taken to rectify the kidney displacement, to prevent its recurrence, and to treat the gastric condition. This may be well done by massage vibrators, which are infinitely superior to hand massage. The genito-urinary symptoms may be referable to the kidney or bladder. Among the former may be hydronephrosis or hemorrhage. Among the latter may be frequency of urination, or even swelling of the vulva associated with a certain degree of fever. Abbot Anderson has never seen a case of the first, but cites cases of the last two. Some patients get well by rest and feeding. Otherwise the treatment, Abbot Anderson thinks, should be directly surgical, or mechanical by suitable trusses or pads.

---

**Tests of the Efficiency of Pasteurization of Milk under Practical Conditions.**—EDWIN HENRY SCHORER and M. J. ROSENAU (*Jour. Med. Research*, 1912, xxvi, 127) report that the thermal death points of pathogenic organisms which sometimes invade milk, have been determined in many laboratories. It has been an open question whether

such results could be translated with safety to the pasteurization of large volumes of milk under commercial conditions. Schorer and Rosenau undertook to determine the effectiveness of commercial pasteurization. Tests were made at a large dairy, in which the method used was the "holding," consisting briefly in heating the milk to 140° to 155° F., and putting it into a receptacle which keeps the milk at this temperature from twenty minutes to an hour. Schorer and Rosenau made 4 tests with 100 gallons of milk. In two, it was planned to heat the milk to 140° F., and in two to 145° F. The temperature attempted was not attained. They tested the efficiency of the apparatus in destroying microorganisms which are most common and serious. In 2 tests with diphtheria, 1 succeeded, 1 failed; in 2 with typhoid, 1 succeeded, 1 failed; in 2 with human tuberculosis, both failed; and in 2 with bovine tuberculosis, 1 succeeded, 1 failed. However, in these cases which failed to kill the tubercle bacillus, only some of the bacteria survived. Fewer guinea-pigs inoculated with the heated milk developed the disease than control animals. The disease was more localized and atypical. From their observations Schorer and Rosenau believe that organisms in milk will be destroyed if heated for twenty minutes at 140° F. Since in practice, milk may not reach even minimum requirements, a liberal factor of safety is necessary commercially. Moreover, the process must not be unduly hurried, thus increasing the physical difficulties of heating all portions uniformly. Finally, Schorer and Rosenau consider official control of pasteurization necessary. It is as important to standardize and guard devices for the temperature recordance of a pasteurization apparatus, as to watch weights and measures.

---

**A New Symptom of Aneurysm of the Aorta.**—R. V. HOESSLIN (*Münch. med. Woch.*, 1912, lix, 24) describes a type of respiration in a patient with aneurysm of the aorta, which is unique, so far as he can discover. The patient was suffering from a gradually increasing compression of the left bronchus. With the growth of the aneurysm the trachea became involved in the pressure. For two days preceding death, the inspiration was stridorous and somewhat prolonged, the expiration interrupted. It was found that the interruptions were synchronous with diastole. The phenomenon is somewhat analogous to interrupted vesicular breathing. In the latter, however, the interruptions are synchronous with systole and occur during inspiration. The cause of the "diastolic expiration," as V. Hoesslin designates the condition, is clear. The compression of the trachea had progressed to such an extent that air could escape from the lungs only during diastole, when the sac diminished in size.

---

**Röntgen Examination and Glycyl-tryptophan in the Diagnosis of Cancer of the Stomach.**—C. KAYSER (*Deutsch. med. Woch.*, 1912, xxxviii, 551) finds that the interpretation of the glycyl-tryptophan test of Neubauer and Fischer is facilitated by röntgenologic studies of the stomach. From a study of 50 gastric cases, he arrived at the following conclusions: (1) The diagnosis of gastric carcinoma is simplified both by Röntgen ray examination and by the glycyl-tryptophan test of Neubauer and Fischer. Cases of cancer have been recognized by these means which

would otherwise have been missed because of the anatomical position of the tumor. (2) All cases, in which Röntgen examination and the tryptophan reaction were positive, were advanced cases of cancer. Whether the two procedures make possible an early diagnosis remains to be seen. (3) A positive tryptophan reaction makes carcinoma highly probable though a negative test does not exclude malignant disease. (4) Where the suspicion of carcinoma is strong clinically and the test is negative, it is necessary to repeat the test a number of times to avoid confusion, for the tumor may at times secrete insufficient ferment to yield a positive reaction.

---

**A simple Method for the Determination of Uric Acid in the Blood and in other Colloidal Fluids.**—F. GUDGENT and E. APOLANT (*Deutsch. med. Woch.*, 1912, xxxviii, 603) have devised a simple method for the determination of uric acid in blood and other colloidal fluids. It has been shown by Gudgent that uric acid exists in the blood only as monosodium urate, a salt which is dialyzable. By experiment he has demonstrated that none of the uric acid is in combination with protein. The authors' method is carried out by dialysis. They find that it can be performed with only 20 c.c. of blood and that the duration of the dialysis need not exceed three hours. (The simple apparatus which is required may be obtained from A. Eberhardt, Berlin, Platz vor dem neuen Tor 1a). *Method.*: After the patient has been on a purin free diet two to three days, at least 20 c.c. of blood is withdrawn from a vein. Coagulation is prevented by the addition of a small knife-point of sodium fluoride. Place 40 c.c. of distilled water in the dialysis cylinder and 20 c.c. of blood in the fish-bladder condom (used as the dialyzer). The latter is hung in the water, so that the level of the blood is a few millimeters above that of the water. The cylinder is now closed with a cork, which at the same time catches and seals the neck of the condom. The apparatus is left at room temperature for two hours, when the water is drawn from the cylinder into an evaporating dish acidified with 6 to 10 drops of dilute hydrochloric acid. Again, 40 c.c. of distilled water are placed in the cylinder and the dialysis is allowed to continue two hours longer. The dialysate is drawn off, and the process repeated a third time. The 120 c.c. of dialysate in the evaporating dish are now carefully evaporated to dryness on a water bath and the murexide test is applied directly to the residue in the dish, as follows: A few drops of dilute nitric acid are placed in the dish and evaporated on a water-bath (not over the free flame). The dish is allowed to cool, several drops of ammonia are added, and again evaporated carefully. If uric acid is present, the residue in the dish is stained purplish red. On the addition of sodium or potassium hydrate, the color changes to reddish blue or violet. For quantitative determinations the method has not proved to be of value. The intensity of the murexide test is no index of the amount of uric acid present. The method is of value in the differential diagnosis of gout and certain forms of rheumatism, which resemble gout clinically. In about 200 gouty patients whose blood has been examined for uric acid quantitatively by the method of Krüger-Schmidt, it has been found that the blood is generally saturated with it (about 8.3 mg. of monosodium urate per 100 c.c. of blood).

## S U R G E R Y

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**General Toxicity of Extracts of Hypertrophied Prostate.**—LEGUEU and GAILLARDOT (*Jour. d'Urolog.*, 1912, ii, 1) have made a biological study of the problem of hypertrophied prostate by experimentation on dogs. These experiments were carried out by injecting a prepared substance containing material from the hypertrophied prostate of man in 10 experiments, from the hypertrophied prostate of the dog in 2, from a uterine fibroid in 1, and from an adenoma of the breast in 1, or with pathological tissues in 14. They were done with the normal prostate of the dog in 10, and the normal prostate of the horse in 2. There was a great difference in the toxicity of the various extracts employed. While with doses as large as 2 grams to the kilogram of animal weight, from the normal prostate of the dog as from the uterine fibroid or adenoma of the breast, no death occurred; on the contrary, in employing the pathological prostate of man, the animal was killed, twice with the dose of 1 gram to the kilogram, three times with the dose of 0 gr. 50, and seven times there were accidents more or less grave out of the 12 experiments. The normal prostate of the dog is less toxic for the dog than that of the horse, while the hypertrophied prostate of the dog is as toxic for the dog as the hypertrophied prostate of man, both being very toxic. Therefore, when a prostatectomy is done, a mechanical obstacle to the bladder is removed as well as something which has a local or general toxic effect on the patient.

**Experimental Researches Concerning Ulcerations of Large Arteries from Contact with Drains.**—WEISSENBAACH and BERTIER (*Archiv. gén. d. Chir.*, 1912, vi, 754) say that the study of the ulceration of arteries, especially of large trunks, to their knowledge, has never before been combined with an experimental research. Humbert and Monod differ as to the cause of the condition. Monod believes in the inflammatory action and necrosing effect of the pus. Humbert attributes the important role to certain adjuvant conditions, particularly to drainage tubes too long maintained in the wound. The direct cause of this paper was a sudden, severe hemorrhage from the wound, following an operation for the removal of an adherent and inflamed appendix. The drainage tube was removed on the sixth day, when the patient was doing well, and two hours later the operator was



summoned hastily. Re-opening the wound was considered but was postponed because the hemorrhage had stopped and the patient was in a grave condition, dying soon afterward. The autopsy showed the pelvis and right iliac fossa filled with blood clots, and an opening in the external iliac artery at the site where the drainage tube pressed on it. Nine experiments, varying in details, were performed on dogs. By operating with strict asepsis in sound tissue and on a healthy artery, they were unable to produce ulceration of the vascular walls by simple contact of the drain or even with continuous and prolonged contact. If traumatic ulceration is possible from escharotic action or necrosis, it is only under very special conditions. The experimental work permitted the writers to emphasize the importance of the role of infection in the so-called traumatic ulcerations; the importance, no less great, of the role played by the drain as an agent for localizing the infection upon the artery, the rupture being only the mechanical consequence of the acute localization of the arteritis; and the necessity of intimate contact between the artery and the drain. Finally, from a practical point of view and so far as one can generalize for man, the experimental facts observed on the animal, these facts confirm what has been observed clinically. It is never necessary in the presence of infection, to permit a drain to remain in contact with an artery more than three days or even two days. If left longer, the mechanism outlined can provoke an ulceration of the vessel.

---

**Surgical Treatment of Genital Tuberculosis in the Male.**—LAPEYRE (*Archiv. gén. d. Chir.*, 1912, vi, 774) says that the operative treatment of genital tuberculosis in the male has made an important advance, and that abstention is no longer the rule. Genital tuberculosis in the adult in its primitive form, is frequently a local, benign, and essentially surgical affection. In the absence of pulmonary and vesical tuberculosis, not only exposed but concealed foci in progressive evolution, should be operated on early. An operation passing beyond the lesion is the method of choice with two exceptions. One should try to preserve the testicle in 50 per cent. of the cases, and he should let alone prostatovesicular lesions of mild grade, because they tend toward spontaneous cure. The operation of choice in the great majority of cases is vaso-epididymectomy, sufficiently but not excessively extensive. Resection of the sound vas deferens, in these cases, should be done systematically in order to save the second testicle (especially after loss of the first). Vaso-vesiculectomy, a rarer operation, should be done. It is of next importance to vaso-epididymectomy. The inguinal and perineal paths are clearly indicated. Bilateral castration should be done only in cases of absolute necessity. Extirpation of the whole genital tract, made grave by the removal of the prostate, is only an exceptional indication.

---

**The After-treatment of Excision of the Knee with the Aid of Approximation of the Bones by a Screw Splint.**—KOLB (*Zentralbl. f. Chir.*, 1912, xxxix, 812) says that the plaster cast, with or without a window in it, is employed by most surgeons. Kolb recommends an apparatus consisting of a metal splint made up of two pieces, one fitting and

sliding into the other and fixed at various lengths by a middle screw at each end. In the excision the bone surfaces are sawed straight and at right angles with the long axis of the bone. A hole is then bored in the lower end of the femur and one in the upper end of the tibia for the screws which are to fix the splint to the bones. The two pieces of the splint are made movable by loosening the middle screw, and are applied to the bones so that the holes in the ends are just over those in the bones, for the introduction of the screws. After these have been introduced and each splint piece has been screwed to the corresponding bone, the sawed surfaces of the two bones are pressed together in good position and the middle screw is made tight. The end screws are prevented from slipping in the holes of the splint by a small lateral screw for each. This permits the splint to be held away from the bones by the end screws, so that it remains 2 to 3 cm. above the skin surface. This renders the changing of dressings very easy. The limb is finally laid on a Volkmann's splint. In 4 out of 5 cases in which the method was employed, good bony union was obtained. In the fifth case amputation was later necessary, because of the general condition of the patient.

---

**After-treatment of Excision of the Knee.**—MERKENS (*Zentralbl. f. Chir.*, 1912, xxxix, 949) following Kocher, does away with all means of fixing the bone ends, aside from that furnished by the bandage. The end of the femur is sawed convexly, that of the tibia concavely. He advocates cleansing the joint cavity; division of the flexor tendons in children; adaptation of the bones; and the introduction of skin and fascial sutures. He believes ligation of the vessels is usually unnecessary, and, if possible, that no drainage should be used. While the bones are held in extension and closely together by a reliable assistant, the knee region is surrounded by a gauze-cotton dressing. The tourniquet is loosened. A plaster cast is then applied including the foot and the pelvis and extending to the umbilicus. The fixation is so good that on recovering from the narcosis the patients have no pain. If the cast presses anywhere this should be corrected. It is not removed for six to eight weeks when bony union is complete, and after removal of the skin sutures it is replaced by a lighter cast. If necessary to expose the wound a window can be made, although this will rarely be necessary. The good fixation and absence of suture material favors the primary union. Merkins regards the Kolb-Wilms apparatus as complicated.

---

**The Technique and After-treatment of Excision of the Tuberculous Knee.**—RIEDEL (*Zentralbl. f. Chir.*, 1912, xxxix, 1125) describes the operation which he calls a radical one. The transverse Volkmann incision extends to 1 to 2 cm. from the posterior surface of the knee on each side, and at each end is combined with a longitudinal incision extending about 6 cm. above and below. The sawing of the bones is begun with the limb extended to favor a correct position of the limb later, but is carried only to a depth of about 2 cm. The knee is now flexed for the first time and the sawing completed. After thoroughly cleansing away diseased tissue and ligation of all visible vessels, the

limb is elevated, and the tourniquet removed. After about fifteen minutes the limb is brought down and the patella which has been sawed transversely, is united by three thick catgut sutures passing around the bone. Then the transverse incision is sutured with catgut and the longitudinal wounds left open. No drainage is employed. An attendant on the operating table holds the limb vertically without traction on the foot. The sawed ends of the bones are fitted together and the knee is surrounded smoothly by one gauze layer after another, winding them firmly. Then follow the layers of gauze covering the limb above and below about 20 cm. from the wound. Upon the gauze are laid sterilized, very thin wooden splints (40 cm. long, 2 or 3 cm. wide, and 1.5 mm. thick) and more gauze is wound around them. When the bones are thus secured the attendant leaves the table and the limb is brought to the horizontal. A support is placed under the pelvis and the limb is covered with gauze, over these being placed long flexible wooden splints. Then the whole limb from the foot to the pelvis is wrapped in cotton in which is incorporated a thick wooden splint on the outer side. This is fixed as far as the waist by a bandage. Finally a Volkmann splint is applied to the knee. This dressing is allowed to remain in position six weeks, and at the end of that time it will be found almost always that union of the bones has taken place. The transverse wound is healed firmly, and at the site of the longitudinal wounds are strips of granulation tissue, which quickly heal over after removal of the granulations. Riedel emphasizes three details: (1) The sawing through the bones while they are in the horizontal position. A mild genuvalgum, more marked in women with their broader pelvises than in men, is the normal position. (2) The first short bandage should be applied with the limb in the vertical position. (3) The dressing can be permitted to remain in position until union is complete because no foreign body (silk ligatures, drainage tubes) are left in. Riedel never employs a plaster cast.

---

**The Technique and After-treatment of Excision of the Knee.**  
—KAUSCH (*Zentralbl. f. Chir.*, 1912, xxxix, 1125) offers a contribution from his experience with excision of the knee, because his methods differ from the preceding in essential points. He observes the teaching of Mikulicz's clinic, making a transverse incision and sawing through the patella. Occasionally, he makes other incisions in order to follow and excise fistulæ. Like Riedel, he emphasizes the necessity of a radical procedure. He always saws the femoral condyle convexly and the tibia concavely. This curved sawing, while not easy, is not very difficult but requires a thin-bladed saw. Whenever possible, it should be so done as not to require correction, but when correction is necessary it can be done best by a large file with an even convex surface. The physiological valgus position should be preserved. It is not necessary that the sawed surfaces should be in exact apposition, nor does it do any harm if the removal of a focus leaves a hole or if there remains a defect in the intercondyloid fossa. The curved sawing usually permits the removal of the bone foci without taking away much bone, in consequence of which there is less shortening than when the sawing is done in a straight line. As a rule, the femur is more involved

by the disease than the tibia, and the outer surface of the bone more than the inner. Anteroposterior gliding is prevented by the curved surfaces of the ends of the bone and lateral gliding by the suturing of the patellar fragments with wire, after sawing from it a transverse piece corresponding in width with the shortening in the limb. Its posterior surface is also sawed off and the patella nailed to the lower end of the femur in order to keep the ligamentum patella tense. Drainage is employed only when there is severe mixed infection. A well padded posterior splint is applied, which extends from the buttocks to the heel. The limb is now brought down to the table without fear of dislocating the fragments. An anterior plaster and hemp splint is prepared which reaches from the toes to the inguinal region, and is applied firmly to the limb. The patient is returned to bed and the limb suspended by means of a ring in the anterior plaster-hemp splint. In the evening or at the end of twenty-four hours the plaster splint is removed and the rubber bandage, applied about the operative field to control oozing, is removed. The plaster splint is then replaced. The whole dressing remains in place for four to six weeks, when it and the skin sutures are removed.

---

**Intravenous Administration of Sublimate, Hyrgolum, Oxycyanide, and Sublamine, in Salvarsan Relapses.**—HEIDINGSFELD (*Amer. Jour. Urolog.*, 1912, viii, 434) says that despite the fact that salvarsan is the most efficient present day remedy for the successful treatment of syphilis, it does not possess, in itself, properties of unfailing efficacy. For a time he relied exclusively upon salvarsan to effect a cure, except in such cases as had received mercurials and other forms of anti-syphilitic medication prior to the administration of salvarsan. The study of these cases reveals that many patients who had received some form of previous medication showed a negative complement fixation test of more prompt and permanent character than those who had received previous treatment of this kind. An effort was made to determine a more effective method of combining the mercurial with the salvarsan treatment. Intravenous administration of bichloride was made in 11 cases; of hyrgolum in 92; oxycyanide in 114; and sublamine in 15. Five cases progressed to an absolutely negative Wassermann under the intravenous administration of hyrgolum, 4 under the intravenous administration of oxycyanide, 6 under the influence of both oxycyanide and hyrgolum, and 1 under the influence of sublamine. Ten cases have shown material improvement and the rest remained unchanged, or have been observed too short a time to permit an estimation from the complement fixation standpoint. Sixteen cases, or 23 per cent. of the 69 cases which have failed to promptly become negative under salvarsan and mercurials in other form, have become Wassermann negative, and 10, or almost 15 per cent. have shown material improvement. These results are relatively low because many of these cases have been treated too short a time to determine the character of the Wassermann reaction. The writer feels sufficiently encouraged to recommend this method of treatment for further observation, study, and confirmation at the hands of others who are engaged in the treatment of these cases. He can only recom-

mend the oxycyanide of mercury when administered in dilutions of 1 to 1000, and in dosage not exceeding .02 gram. Great care should be exercised in its careful and proper administration. The vein must be carefully and properly entered without incision, to prevent disfigurement. Great care must be exercised not to produce an effusion of the remedy outside the vein. Such an accident while not immediately as painful as that of salvarsan, is prone to produce an inflammatory infiltration of rather severe and distressing character. A wider, more extensive experience and a more prolonged and careful observation, will determine to what extent it can be employed as a routine measure in the successful treatment of syphilis.

---

**The Value of Direct Gastroduodenoscopy in Affections of the Stomach and the Duodenum.**—ROVSING (*Annals of Surgery*, 1912, lvi, 201) ventures to assert that we have obtained in the direct gastroduodenoscopy described a method which, in those difficult cases where all other diagnostic expedients are insufficient, enables us to give the exact diagnosis in cases of disease in the stomach and duodenum. It is of special importance in three directions: (1) In the numerous cases where the symptoms speak in favor of ulcers, but where inspection and palpation of the stomach show nothing of the sort. Here gastroduodenoscopy removes all doubts, and sometimes shows us that the supposed ulcer does not exist, whereby the patient is spared a senseless and injurious encroachment; and sometimes it proves the presence of the ulcer, its seat, and its nature. (2) For the differential diagnosis between ulcers in the stomach and the duodenum. (3) By rendering possible a direct attack upon the ulcer, where one had formerly to content himself with gastro-enterostomy because the seat of the ulcer was unknown. This is of exceptional importance with ulcers, the hemorrhages from which constitute a menace to life whether there be permanent oozing, small bleedings, or violent, acute hemorrhages. Nor, naturally, is this method infallible; as with it also one may sometimes overlook a small ulcer which has concealed itself in the folds of the mucous membrane, and may sometimes interpret a depression as being the edge of an ulcer or something similar, but this is of rare occurrence.

---

## THERAPEUTICS

---

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

---

**Luminal—A New Hypnotic.**—GOLDSTEIN (*Deutsch. med. Woch.*, 1912, xxxviii, 987) believes that solutions of luminal are changed by boiling, and therefore the remedy is much less active when given subcutaneously.

The administration of the remedy by mouth is often impossible because of its intense bitter taste. He believes that the best effects are obtained when it is given in the form of suppositories. Thus in 79 per cent. of his cases sleep was induced when luminal was given by rectum, and in only 50 per cent. when it was given subcutaneously. Luminal acts slowly, according to Goldstein, requiring from one to two hours before sleep is produced. He believes that it is twice as active as veronal, but decidedly inferior to adalin as a sedative.

---

**The Action of Salvarsan and Neosalvarsan on the Wassermann Reaction.**—McDONAGH (*British Med. Jour.*, June 8, 1912, p, 1287) gives his observations on the value of the Wassermann reaction as a guide to the treatment of syphilis. In the primary stage, when the reaction is negative before treatment is commenced, most cases give a positive reaction afterwards. This reaction is most marked about the forty-eighth hour. In some cases, on the other hand, the reaction does not become positive until the fifth day. Although it may remain positive for several days, the degree diminishes generally about the third week, until it becomes negative before the eighth week. If the reaction is only slightly positive after the injection, it becomes negative much earlier. If the first injection gives rise to only a weak reaction then three or four more will undoubtedly suffice to make the reaction permanently negative; if, however, the reaction is strong, then the patient is in the secondary stage, and will require at least 3 grams of salvarsan or neosalvarsan before the desired effect is obtained. In the secondary stage when the reaction becomes strongly positive after an injection, and in cases in which it is markedly positive before treatment is commenced, no blood tests need be made until before and after the fourth injection, as in McDonagh's experience the four injections are the minimum likely to be required to produce a permanent negative result. In the tertiary stage the Wassermann reaction behaves much in the same way as it does in the primary and secondary, except for one peculiar phenomenon, which is occasionally to be noted—that is, a case with a strong positive reaction before treatment may become negative immediately after an injection and remain so from twenty-four to seventy-two hours, and then becomes quite positive again. Patients who have had syphilis and give a negative Wassermann reaction are either cured or in the latent stage, which of the two can only be ascertained by giving a provocative injection of salvarsan and then testing the blood. As an injection of salvarsan will not give rise to a positive reaction in a non-syphilitic, one must regard the occurrence of such as indicative of the presence of disease, and efforts should be made to bring about a cure. Taking all stages of syphilis, McDonagh has found that three to seven injections are necessary to cure most cases of syphilis. There is no doubt that many cases in the tertiary stage can be cured with neosalvarsan which failed to be cured with salvarsan. Liable to change as these conclusions may be, he cannot but admit that the alterations in the Wassermann reaction as the result of treatment are most constant, and when tested at short intervals, give a much safer guide to regulate treatment than by saying that just so many injections will be required, or, as the old syphilologists used to teach, that a three years' pill treatment was

sufficient for all cases alike. As there is a possibility of fallacy, he advises his patients to have a provocative injection of neosalvarsan six months or a year after they have been discharged, and the blood tested forty-eight hours, the seventh, fourteenth, twenty-first, and twenty-eighth day after that injection.

**Influence of Salvarsan Treatment on the Wassermann Reaction.**—MÜLLER (*Wien. klin. Woch.*, 1912, xxv, 873) notes the results of the Wassermann test in 85 cases of syphilis in the secondary stage treated with injections of salvarsan and observed for a considerable period of time after the treatment. The Wassermann test gave a negative response in from four to eight weeks after the injections in the majority of cases, but in more than half of these the reaction became positive again from three to twelve months later. In some cases the disease ran a malignant course with a constantly negative Wassermann reaction. One patient had been persistently treated for over two years with every known means of combating syphilis, but has never been free from manifestations of the disease for a single week, and yet the Wassermann test was always negative throughout. In another malignant case mercury proved ineffectual, but under salvarsan the manifestations of the syphilis temporarily subsided, while at the same time the previously constantly negative Wassermann findings became positive. The findings seem to indicate that although salvarsan has a more rapid therapeutic action on syphilis than mercury, yet it does not ensure a permanent cure.

**Lumbar Puncture in the Treatment of Uremia.**—FREY (*Correspond. Blatt. f. Schweiz. Aerzte*, 1912, xlii, 623) treated 8 of 20 cases of acute uremia by lumbar puncture and permanent benefit resulted in all but 2 cases in which the process was too far advanced to hope for even temporary benefit. In 1 case reported in detail repeated venesection had failed to relieve, but the beneficial effect of lumbar puncture was prompt and lasting. Frey believes that probably the effect of lumbar puncture is largely due to relief of mechanical pressure, although the removal of toxins may be an element. Frey notes that the symptom-complex of uremia is dependent upon many different factors. If the principle factor is retention by the kidneys, marked benefit will be derived from infusion. If the symptoms are largely dependent upon cardiac weakness, venesection will be of great value. It is in the type with marked cerebral symptoms that lumbar puncture will often be of great value toward saving life.

**Clinical Experience with Luminal.**—LOEWE (*Deutsch. med. Woch.*, 1912, xxxviii, 947) says that luminal is a valuable sedative and hypnotic in all forms of insanity and also in excessive irritability and insomnia occurring in the course of neurasthenia. It is a very useful hypnotic when other hypnotics fail or are contraindicated. In cases of delirium such as delirium tremens, luminal exerts a sedative action in much smaller doses than are necessary with veronal. It is given as a hypnotic to normal individuals in doses of usually 0.2 gram and at the most 0.4 gram is necessary to secure physiological sleep. The remedy has been given in much higher doses in insanity without

apparent ill effects. Untoward effects such as fall in blood pressure intoxication symptoms, and habit formation are seen only in long-continued usage of the remedy, and are very similar to those produced by veronal. Luminal may be given by mouth in tablet form or the sodium salt of luminal which is easily soluble in water may be given in solution. The sodium salt may also be given by rectum, but it is especially valuable in that it may be given hypodermically. Loewe says that the combination of small doses of morphine with luminal is as effectual as hyoscin except its action is not so prompt.

---

**The Salvarsan Treatment of Pernicious Anemia.**—BRAMWELL (*British. Med. Jour.*, June 22, 1912, p. 1413) adds to a previous communication in which he reported 2 cases of pernicious anemia much benefited by the administration of salvarsan. These 2 patients have remained apparently well for over a year without any further treatment. He reports 5 other cases treated on the same plan. One of these 7 cases showed very striking improvement, four injections of 0.3 gram each being given during a period of six weeks during which time the red blood cells increased from 1,760,000 to 3,350,000 and the hemoglobin rose from 52 per cent. to 78 per cent. During the year following the last injection the blood continued to improve steadily, the red blood cells increasing to 6,210,000 and the hemoglobin rising to 120 per cent. Five other patients showed more or less improvement, and in only 1 of the 7 no benefit whatever was derived from the treatment. Bramwell believes that the beneficial effects were definitely dependent upon the salvarsan and not a coincident. He is of the opinion that salvarsan is a more efficient remedy than arsenic given by mouth. To secure the best results salvarsan should be given intramuscularly, on account of the prolonged action which results from its slow absorption when so given.

---

**The Treatment of Scarlet Fever with Salvarsan.**—KLEMPERER and WORTA (*Therapie d. Gegenwart.*, 1912, liii, 198) relate their experiences with the salvarsan treatment of a series of 39 cases of scarlet fever of severe type. They compare the results they obtained with cases occurring in the same epidemic treated by the usual symptomatic method. They were led to try this method of treatment because of the curative action of salvarsan in many diseases, not closely related. Among these may be mentioned a group of infections caused by some variety of spirillum, another group caused by animal parasites, and again a number of diseases of entirely unknown origin. Another factor which led them to try salvarsan was that the Wassermann reaction has been found positive in severe types of scarlet fever. Of the 39 cases treated with salvarsan, 5 died, a mortality of 12.6 per cent. as compared with 24.5 per cent. mortality in 44 cases not treated with salvarsan. The percentage of complications was also much smaller in the cases treated with salvarsan. Thus otitis media developed in only 6.6 per cent., as compared with 14.3 per cent. in the untreated cases; nephritis occurred in 25 per cent. as against 43 per cent.; and endocarditis was observed in 3 per cent. instead of 16 per cent. The therapeutic effect of the remedy was marked upon the course of the disease, especially upon



the temperature. In all but 2 cases the temperature fell by crisis shortly after the injection. This fall was followed by a rise on the following day, but seldom to the original height of the fever. A few of the patients received a second injection of salvarsan. The doses given were 0.1 to 0.2 gram to infants, 0.3 gram to older children, and 0.5 gram to adults. Most of the injections were given intravenously and only were given in highly diluted form intramuscularly when intravenous injections were impossible. Klemperer and Woita hope that further experience will confirm their belief in the value of salvarsan in the treatment of scarlet fever.

---

## PEDIATRICS

---

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,  
OF PHILADELPHIA.

---

**Vaccines in the Treatment of Pertussis.**—MAYNARD LADD (*Archives of Pediatrics*, 1912, xxix, 581) reports the results of vaccines prepared from Bordet's bacillus on cases of pertussis. Bordet's bacillus, while not universally recognized, is fairly well established as the causative factor in pertussis. It is a small cocco-bacillus found in the expectoration from the paroxysmal cough of pertussis; it can be grown on serum or blood-bouillon and gives the agglutination and complement test for pertussis. Vaccines from this bacillus were used on selected cases of typical pertussis, the blood counts showing a relative increase in the mononuclear cells. A minimum interval of five days was allowed between injections, but the intervals were often increased to two weeks, as the cases were not brought to the hospital regularly. There were no general or local reactions from the injections, and as many as 40,000,000 bacteria were given as one dose to children aged nine months, and were repeated several times without bad effect. No other treatment but the vaccine was given. All the children recovered without complications on an average in five weeks after beginning the injections. On an average the cases were in the third week of the disease when the treatment was started. The usual, long drawn out course lasting from two to three months was absent. It is believed that by using larger doses at shorter intervals a greater efficiency of the vaccines may be established.

---

**Intestinal Poisoning under the Guise of a Cerebral Affection.**—OSWALD MEYER (*Deutsch. med. Woch.*, 1912, xxxviii, 1550) calls attention to that class of intestinal toxemias occurring in children aged under three years in which the cerebral symptoms hide the true condition and made a correct diagnosis difficult. Many cases of the cerebral type would be saved if the intestinal condition were sus-

pected, and adequate treatment given for it. He describes one case as an example in which the child became suddenly ill with fever, vomiting, convulsions, coma, athetoid movements, and spasticity of the left arm, loss of patellar and pupillary reflex, spasticity of the left side, and conjugate deviation of the eyeballs. The condition continued four days, improving, however, when purgation and colonic irrigation were employed because offensive stools suggested intestinal poisoning. The coma and loss of reflexes persisted for four days, clearing up slowly. The urine was negative. The child recovered under the treatment for intestinal poisoning, and in nine days was well. Conjugate deviation is usually found only in true cerebral conditions, although one-sided convulsions and spasticity may occur in intestinal poisoning. The cerebral localization suggested by the one-sided symptoms can only be explained by a general diffuse irritation of the centres, which had more effect upon certain motor centres than upon others. Meyer mentions a second case in which the long duration of the cerebral symptoms could only be explained by the severe symptoms of intestinal poisoning, the foul odor of the stools persevering for four days even after the cleaning out of the bowel. One should not neglect this possibility of intestinal poisoning in cerebral cases and should not employ chloral too soon or too freely until the intestinal tract is thoroughly cleaned out. If the interval between the onset and the clearing of the bowel be too long the symptoms will continue until the poisons get out of the blood stream. To facilitate the latter the use of normal saline solution is advised.

---

**Massage in Wasting Diseases of Children.**—J. M. MACPHAIL (*British Jour. Child. Dis.*, 1912, ix, 404) reports excellent results in infants with wasting diseases by employing general massage. He holds that wasted babies, particularly in infirmaries and institutions, do not thrive better because they lie inertly most of the time and are not nursed and handled, thereby missing a general manipulation essential to muscular and vascular tone. He describes his results with children in the wards of a hospital. These children were rubbed routinely with codliver oil, but, as many of them did badly, he instituted general massage lasting half an hour, and stretching out all the muscles. He also employed the Schäfer and Sylvester methods of artificial respiration to promote better circulation and prevent stagnation in the lungs. The general and local conditions speedily improved, the muscles became firm, and the children ate and slept better. In one case, a baby aged seven months, wasted from a chronic diarrhea, gained 4 pounds 2 ounces in twelve weeks, and improved markedly. Another case of marked rickets with intestinal catarrh in a baby aged ten months, gained 4 pounds 1 ounce in seven weeks, and showed marked improvement. All the cases were improved by this treatment. Both of the cases cited above gained without any alteration in diet.

---

**The Treatment of Asthma in Children.**—H. E. KNORF (*Berlin. klin. Woch.*, 1912, xlix, 1566) reports 5 cases of asthma in children, all of them cured and with no return of the disease so far. Asthma is found in children more frequently than is commonly believed. The import-

ant part of the treatment lies in teaching the patient to use his muscles of respiration properly. In asthma the thorax attempts inspiration at the same time that the abdomen attempts expiration. All complications of asthma, excepting the nervous forms, are benefited and often cured by this method of treatment. Other therapeutic measures are naturally not neglected, especially the supervision of the child's food, especial stress being laid on having only milk and vegetables for supper and having them eaten early so that the stomach is empty at bedtime. Attention to the child's environment and hygiene are important factors in treatment, and it is advisable that the child be given sanatorium treatment for a short time for its psychic effect. It appears that asthma, like stuttering, sometimes disappears at puberty. The treatment includes psychical influence, development, change of environment, and the teaching of normal breathing by daily breathing gymnastics.

---

**Typhoid Fever in Infancy.**—J. P. CROZER GRIFFITH (*Archives of Pediatrics*, 1912, xxix, 565) gives an analysis of 75 cases of typhoid fever in infants aged two and one-half years and under. The duration of the onset in 44 cases was not over seven days in 58 per cent., and not over five days in 28 per cent. In some cases the onset lasted only two or three days. It was sudden in 35 per cent. and rapid in 27 per cent. of the cases, illustrating the tendency to rapid onset in children. Fever rose rapidly, reaching its height much sooner than in adult life. There is a much greater tendency to diarrhea during the onset in children than in early or later childhood, and this symptom was present in 57 per cent. in this series. Vomiting occurred as an early symptom in 34 per cent. of the cases. Headache was noted in 14 cases, all aged at least two years. Cough was infrequent at the onset, being noted in only 18 cases. Epistaxis is significant by its absence, being noted in but 4 cases. Tympanitis is infrequent at the onset. Abdominal pain or tenderness was noted in but 12 cases. Convulsions were noted in but 3 cases, showing the striking absence of this sign. The symptoms of the developed attack show many digestive signs. Coated tongue is common, anorexia infrequent, and abdominal distention, and bronchitis common. Nervous symptoms are not marked, and the typhoid state exceptional. The course of the fever is not characteristic, being steadily high or moderate, and later often irregular, but it may be irregular from the beginning. The fall is often rapid. The total duration of fever is three weeks or less in most of the cases. Typhoid roseola is common, appears early, from the fourth to the sixth day, and was present in 48 cases. The spleen was enlarged in one-half of the cases. The Widal reaction is characteristic, as in adults. Leukocytosis is absent. The urine often shows albumin and casts. Complications occurred in 31 cases and consisted of exanthemata, 1 intestinal hemorrhage, and 25 per cent. of suppurative processes, the last being a tendency in infancy. Relapses occurred in 3 cases. The type of the cases was rather severe, the mortality being 12 or 16 per cent. The treatment was symptomatic. Tubbing, with the water at 90° or 100° F. is preferred to sponging. The diet was largely milk, including cereal gruels, broth, and beef juice.

## O B S T E T R I C S

---

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

---

**Uterine Scar after Cesarean Section.**—HARRAR (*Amer. Jour. Obstetrics*, May, 1912) contributes an interesting paper upon uterine scar after Cesarean section, by giving the experience of the Lying-In Charity of New York. He reports 3 instances of vaginal delivery in patients who had previously had abdominal Cesarean section, describes the gross appearance of the scar in repeated sections, and reports cases of rupture of the uterus, 4 in number, after one or more sections. Microscopic studies were made of the scar in cases of rupture, and in those cases where rupture had not occurred. He concludes that in undertaking Cesarean section on a patient who has been long in labor, with ruptured membranes, and who may be infected, we must recognize the probability of obtaining a poorly healed scar which would make future pregnancy dangerous. In repeated Cesarean section it is best to excise the old uterine scar rather than make a new incision parallel to it, thus avoiding the isolation of a weakened strip of uterine wall between two scars. In the after-treatment of Cesarean section, should lochia be retained, intrauterine douches should not be given because of the danger of infection and mechanical injury to the uterine wound. In managing a case where Cesarean section has been previously performed for the relative indication, one must be guided by the history of the previous convalescence, as well as by the method of suture employed. We must thus estimate the integrity of the old scar and its capacity to endure the strain of vaginal delivery. The microscopic study, in cases where rupture had occurred, showed that in some patients the normal uterine muscle had not developed in the scar, but had been replaced by attenuated connective tissue, which readily gave way. In other cases rupture occurred through uterine muscle the nutrition of which had been impaired by the adjacent scar.

---

**Rupture of the Cranial Dura Mater in the Newborn.**—MEYER and HAUCH of Copenhagen (*Archiv. mensuelles l'Obstétrique*, March, 1912) report 28 cases of rupture of the cranial dura mater in the newborn occurring in 1200 confinements. In 13 this rupture and hemorrhage were considered the cause of death; 6 of these were still-born, and 7 born living. In 4 cases the child was very large and was extracted by a difficult forceps operation. In 1 case the birth was accomplished by difficult breech extraction. In all, death was the result of this accident in 12 cases in 1200 confinements, or 1 in 100. Hemorrhage is greatest where the rupture is at the tentorium, as there the vessels are most abundant. Rupture through the falx cerebri does not cause great bleeding, and in no case was serious injury observed in the inferior longitudinal sinus. Where the two layers of dura mater

have completely ruptured, hemorrhage is abundant, and the child is still-born. In some instances a large vein is torn across. This accident occurs in spontaneous labor where expulsion occurs very rapidly. In one case the child died from ulcer of the stomach, probably due to hemorrhage some days after delivery. In 10 cases breech extraction produced the accident; in 1 case difficult forceps extraction. Comparison shows that this rupture occurs more often when the child is extracted by the feet and breech than when delivered by forceps.

---

**Prognosis of Repeated Classic Cesarean Section.**—MAIROTON (*Archiv. mensuelles l'Obstétrique*, March, 1912) reports 38 cases of repeated Cesarean section in the Tarnier clinic at Paris. It was found that where the first operation had been done under aseptic precautions, with a correct suture, the risk of rupture in the scar in subsequent labor was not sufficient to cause hesitation in performing section. In the repeated operation, in 7 cases there were adhesions which complicated somewhat the second procedure. In 2 there were adhesions between the uterus and omentum, and in 2 between the uterus and the abdominal wall. There seemed to be no difference in the various sorts of suture material provided they were sterile and properly introduced. Infection is a great cause for adhesions, but this may be so mild as to produce few if any symptoms. Adherence of the membranes to the uterine wall renders delivery more easy; hemorrhage was not observed. It was thought best to excise the old scar at the following operation. In making the repeated section, the operator must be careful in opening the abdomen to avoid the coils of intestine which may be adherent to the abdominal wall. At repeated operation, the question of sterilization must be decided by the circumstances present with each patient. Abortion does not occur as a result of this operation, and a premature labor rarely happens. In 19 cases the patient came into spontaneous labor at term, or was operated upon at term, just before the commencement of labor. In one patient in whom a third operation was done, the uterus was adherent to the surrounding tissues. Mairotton concludes from his experience that the repeated operation is justifiable.

---

**Retroversion of the Gravid Uterus with Over-distention of the Bladder, and Hematuria.**—BARRIS (*Jour. of Obst. and Gynec. of British Empire*, April, 1912) reports the case of a multipara about four months pregnant, who had severe pain in the lower part of the abdomen, and great difficulty in emptying the urinary bladder. As some urine was discharged, and the patient objected to the use of the catheter, it was not employed. The patient continued to suffer with pain in the bladder region and could only pass urine with difficulty. The abdomen increased in size and the legs became swollen. On admission to hospital the abdomen was greatly distended by a tense elastic tumor, reaching within an inch of the border of the ribs. Seven pints of clear urine were withdrawn by catheter. Three and one-half hours afterward, three and one-half pints were withdrawn. On examination the uterus was found pregnant, about three months, lying above the pelvic brim, and extending into the abdomen. It had previously

been displaced by the fingers, the first examination having found the uterus in the hollow of the sacrum. The subsequent treatment of the case consisted in catheterization every four hours and the administration of urotropin. Examination of the urine showed the presence of red blood corpuscles with alkaline reaction. Microorganisms were absent. A rubber ring was worn for some time until the uterus was sufficiently large to remain above the pelvis, and the urine had become normal. The patient's pregnancy went on normally.

---

**Cesarean Section for Dystocia, Due to Coils of the Cord around the Fetus.**—BRIGGS (*Jour. of Obst. and Gynec. of British Empire*, April, 1912) reports the case of a multipara in labor, the fetal head lying transversely above the brim, with the occiput to the right. Labor had been in progress ten and one-half hours, but the cervix admitted one finger only. On the following day the membranes ruptured prematurely, with half dilatation. Progress ceased, and the patient's pains were quieted by morphine. On examination, a short cord was diagnosticated as the cause of delay, and as mother and child were in good condition, delivery was effected by Cesarean section. The fetus weighed 8 pounds, 2 ounces; the cord measured 28 inches in length, and was coiled tightly about the fetal neck. The placenta was implanted on the anterior right wall of the uterus, and in delivering the child a large area of the placenta and its short portion of intact cord were withdrawn. The pallor of the child was threatening at first, but the child was resuscitated when the cord was loosened.

---

**Congenital Graves' Disease, and Total Occlusion of the Duodenum in the Newborn.**—WHITE (*Jour. of Obst. and Gynec. of the British Empire*, April, 1912) reports the birth of a fetus in the first labor of a mother who suffered during pregnancy with characteristic exophthalmic goitre. The child was delivered by forceps, weighing 4 pounds, 6 ounces. It presented the characteristic features of Graves' disease, with exophthalmos and tremor of the hands. The thyroid was enlarged, the heart action very rapid, and a loud murmur was heard over the precordium. The child remained deeply cyanosed. It lived thirty-five hours only. The mother improved, but in a subsequent pregnancy her symptoms again became worse, and she gave birth to a stillborn, premature child, without abnormality. An examination of the body of the fetus showed a large subdural hemorrhage over the right parietal region, extending over the temporosphenoidal lobe. The suprarenals were large, the thyroid enlarged, and an accessory thyroid was found under the root of the tongue. The thyroid substance, on examination, was sterile. Microscopic examination of the thyroid showed proliferation of cells, with colloid material. The second case was that of a normal, and normally-sized male infant born in spontaneous labor from a healthy multipara. At birth there was a large umbilical hernia, whose sac covering burst, exposing the intestine. The lower end of the bowel reached the abdominal cavity through an aperture immediately above the umbilicus, causing sufficient compression to produce congestion in the intestine. The hernia was too large to permit of its reduction by operation. Beginning peritonitis was present. The child took nourishment for some hours,

but later vomited a large quantity of fluid. The meconium was white in color, and a diagnosis of congenital obliteration of the bile ducts was made. The child had seemed to be in constant pain, which was not subdued by morphine. Death occurred after thirty-six hours. On postmortem examination the duodenum ended in a cul-de-sac lined with normal mucous membrane. There was nothing to indicate where the jejunum was attached, but on the outer coat of the blind extremity was a solid cord continuing into the small intestine, of the usual size. The occlusion was not near the neck of the hernial sac. The whole intestine was filled with white cheesy material containing no trace of bile.

---

## GYNECOLOGY

---

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

---

**Kidney Changes Following Sudden Occlusion of the Ureter.**—In view of the varied and often diametrically opposite statements as to just what happens to the kidney after occlusion of the ureter, which are to be found in the standard text-books, and of the by no means infrequent occurrence of injury to the ureter during gynecological operations, several studies of the subject from the experimental and clinical standpoint, which have recently been reported, are of interest. KAWASOYE (*Zeitschr. f. gyn. Urologie*, 1912, iii, 172), whose investigations as to the best method of permanently occluding the ureter, when it is desired to do this, have already been reviewed in these pages, has examined the kidneys in a series of 10 rabbits killed from two to seventy days after the ligation of one ureter. He found a hydronephrosis of the corresponding kidney in every instance, this being greater in amount the longer the time which had elapsed between the operation and the death of the animal. Up to the fourteenth day he found an increase in the weight of the parenchyma, due to retained urine in the tubules; after this time atrophy occurs. The chief microscopic changes noted were hyperemia, dilatation, and atrophy of the tubules; complete disintegration of the entire parenchyma did not occur in any of his experiments, but he believes that that would doubtless have been the end result, had any of the animals been permitted to live long enough. In a similar series of experiments, where the ureter was loosely tied, but not completely occluded, no hydronephrosis was produced, merely a marked dilatation of the ureter above the point of ligation. A third series of experiments was undertaken to ascertain how long a ureter can remain completely occluded without the kidney losing its integrity. It was found that if the ureteral obstruction is removed in from two to four days, the kidney undergoes complete functional regeneration, as judged by the indigo-carmin test; partial regeneration may take place up to one or two

weeks, but after three weeks no secreting power whatever could be demonstrated. Quite similar experiments have been performed on 30 dogs by SCOTT (*Surg., Gyn. and Obstet.*, 1912, xv, 296). In some of these he produced a permanent, in others an intermittent obstruction, by ligating the ureter with a rubber band, tight enough to produce complete obstruction until the pressure in the pelvis of the kidney became sufficient to stretch the rubber band and let the fluid escape. He also found that complete obstruction to the ureter always causes hydronephrosis, the degree depending upon the duration of the obstruction; intermittent obstruction has the same effect, but does not act so quickly. He found the chief changes in the parenchyma to be dilatation, first of the straight tubules, then of the convoluted tubules, and lastly of the glomeruli. His experience has been that in even the highest degree of hydronephrosis the kidney epithelium is never entirely destroyed, but is capable of further secretion; in only one of his cases of incomplete, and in no case of complete obstruction, did atrophy of the kidney occur. A study of the same subject, from the clinical as well as the experimental side, is reported by BARNEY (*Surg., Gyn., and Obstet.*, 1912, xv, 290). He has collected from the literature and by personal communication 62 cases of sudden and complete ligation of the ureter by ligature or clamp, most of these having occurred during a vaginal or abdominal hysterectomy. In 46 of these cases the occlusion was unilateral, in 16 bilateral. In 20 per cent. of the former, no symptoms whatever, either immediate or remote, were noticed, the patients making a complete and uneventful recovery. In but 1 case of unilateral obstruction did anuria and death follow. This agrees with Barney's experimental results, unilateral ligation of the ureter in 26 dogs and 7 rabbits failing in a single instance to produce this renorenal reflex. In 26 per cent. of the cases of unilateral obstruction observed clinically there was some transient pain or tenderness in the kidney region, but only in one instance was this so persistent as to necessitate a subsequent nephrectomy. In no case of bilateral ligation was any pain produced. Barney believes that where pain is produced this is probably the result of intense renal congestion, with stasis of urine; owing to the formation of anastomosing vessels, providing new channels for the venous circulation, this congestion gradually subsides, and the pain is relieved. In 24 per cent. of the clinical cases, urinary fistulae established themselves, an occurrence which was never noted in the experimental work. In 15 per cent. of the unilateral ligations, infection of the corresponding kidney followed, but this was never seen in the bilateral cases. Experimentally, Barney also has found that ligation of one ureter is practically always followed by the development of hydronephrosis. In only 15 of the clinical cases was the subsequent condition of the kidney noted, but in 12 of these hydronephrosis was present. In most of them the obstruction was relieved before many days had elapsed, so that no large sacs were encountered. In one instance the obstruction was not released until ten days after the operation, but then the kidney took up its normal function, apparently unimpaired; the same was true of several others in which the occlusion has lasted from five to six days. From these facts, and the results of experimental work, Barney concludes that after the release of a ureter long obstructed, the kidney usually displays



remarkable recuperative power; an organ which at first appears of little value may prove an important factor in the elimination of metabolic waste, so that unless a kidney under these circumstances is definitely proved worthless, nephrectomy should not be hastily performed.

**Operation for Carcinoma of the Vulva.**—STOECKEL (*Zentralbl. f. Gyn.*, 1912, xxxvi, 1102) calls attention to the almost uniformly bad results that are obtained in the surgical treatment of vulvar carcinoma, and to the lack of any serious efforts to improve them, comparable to those which have been expended on carcinoma of the cervix. He believes that these bad results are due chiefly to the very early metastases caused by this form of carcinoma in the regional and more distant lymph glands, together with the age and poor general condition of many of the patients. The glands principally affected are the inguinal, iliac, and hypogastric. Although the latter can be reached extraperitoneally by a pararectal incision, Stoeckel prefers to approach them transperitoneally after opening the abdomen in the midline, as this permits of a better view and more thorough extirpation. Having removed as thoroughly as possible all the pelvic glands, the laparotomy wound is closed, and two long oblique incisions are made, starting at each anterior superior spine, and meeting in an obtuse angle over the mons veneris. Through these the inguinal glands with their surrounding tissue are removed in one mass, care being taken to clean out the triangle between the sartorius and pectineus down to the fascia and vessels. This accomplished, the next step is to make a vertical incision from the mons veneris downward, passing around the vulva, and then to shell out the entire vulvovaginal tissue, keeping close to the anterior surface of the symphysis and the internal edge of the pubic arch. Only after complete freeing of the vagina from the urethra, from the pubic bone, and from the rectum, is the tumor mass finally cut away. All wounds are closed with fairly free drainage, and a permanent catheter is placed in the bladder. Stoeckel believes that if every case of vulvar carcinoma, in which there is the slightest chance of radical extirpation, were subjected to this operation, carried out under spinal anesthesia, the percentage of permanent cures would be much higher than it is at present.

**Trauma as a Factor in Rupture of Pyosalpinx.**—Three interesting cases of the rupture of a pyosalpinx, in which the immediate cause appeared to be a single acute trauma, are reported by JAWORSKI (*Gyn. Rundschau*, 1912, vi, 478). The first case was that of a woman, aged thirty-six years. Several workmen were carrying a piano out of her house, and appeared to be letting it fall, when the patient sprang forward and made a violent effort to help lift it. She immediately fell to the ground in a faint; in a half hour vomiting set in, accompanied by clammy sweat. In a few hours she died, and at autopsy both tubes were found transformed into pus sacs, the left one containing an area of rupture the size of a dollar. Death was due to acute peritonitis. The second patient was aged forty years. On the third day of a menstrual period she was seized with sudden, lancinating pain in the lower abdomen immediately after lifting a heavy wash-tub.

She fell unconscious; this was followed in her case also by vomiting and collapse. Death occurred the same night. At autopsy an area of rupture the size of a bean was found on the anterior wall of a left pyosalpinx, accompanied by an acute pelvic peritonitis. The third patient was aged forty-two years. She was seized during the act of coitus, performed during the menstrual period, with lancinating pains, followed by violent vomiting, and died on the following day. At autopsy bilateral pyosalpinx was found, with acute peritonitis. In the mid portion of the right tube was an opening from which thick, yellowish pus was discharged. In all these cases the rupture occurred after physical exertion, which was accompanied by increased abdominal pressure. In 2 menstrual congestion seems to have played some role, and Jaworski believes that the congestion attendant upon coitus may also be at times an important factor. The extreme gravity of rupture of an acute pyosalpinx is well illustrated by these 3 cases, in every one of which the patient died inside of twenty-four hours. In one case operation was advised, and refused, but in the others the condition of the patient was so desperate from the start that operative interference could not be considered.

---

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

---

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA.

---

**Carcinoma of the Tongue Treated by Adrenalin.**—HOLSCHER reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 7 Livraison, 1912) a case of carcinoma of the tongue, the size of a hen's egg, which had necessitated tracheotomy. He commences by injecting a few drops of adrenalin, gradually increasing to 2 grams a day. As a result, the tumor began to undergo gangrene and to be thrown off in part. At the moment of presentation there existed only a very small tumor at the base of the tongue.

**Farcy (Glanders) of the Larynx and Pharynx.**—MAHU reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) a case of pharyngolaryngeal farcy in a veterinary surgeon, aged thirty years, whom he had treated for two months for grave ulcerations of the larynx and pharynx in sequence to an infection of glanders beginning with pleuropneumonia, followed by abscesses localized in the anterior portions of the limb and the adductors of the thigh. All treatments, topical and general, had been without result. Poyet had occasion to see a case of laryngotracheal farcy in a veterinarian. He found the larynx ulcerated at its anterior portion with invasion of the arytenoids, and ulceration of the anterior portion of the trachea. At the autopsy an uninterrupted ulceration was seen

to extend from the larynx to the bifurcation of the trachea, with a perforating ulcer at that point which had been the immediate cause of death.

---

**Asphyxia from Descent of Excised Adenoids in the Trachea, Revealed by Bronchoscopic Intervention.**—GUISEZ, in a recent paper read at the French Congress of Otology, Rhinology, and Laryngology (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912), upon the escape of adenoid vegetations in the air passages, reported several cases of his own observation. In 3 of them the presence of the vegetations was revealed by bronchopulmonary manifestations, which in 2 instances ensued after emesis and ejection of the vegetations at the end of ten to fifteen days. In another case the offending body was removed under bronchoscopic intervention. Finally, quite recently, Guisez had been called to an infant in a paroxysm of asphyxia from which it was freed by the removal of a mass of vegetations which straddled the bronchial spur.

---

**A New Method of Plastic Injections.**—BRÜNINGS (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911) describes a new method to supersede paraffin injections in saddleback noses and similar deformities by substituting fat tissue taken from the body of the individual. One advantage is that the fat remains in position without shifting, as the paraffin sometimes does.

---

**Radical and Aseptic Cure of Frontal Sinusitis by Plugging the Sinuses.**—TORRINI describes (*Revue Hebd. de Lar., d'Otol. et du Rhinologie*, December 9, 1911) a new radical procedure for the cure of frontal sinusitis, avoiding the disfigurement produced by other methods. He raises the periosteum, destroys the anterior wall of the sinus, cures the interior, enlarges the infundibulum, and then plugs the cavity with the lead paste of Beck, replacing the periosteum.

---

**Nasal Stenoses.**—For the prevention of nasal synechia, MOURE (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) interposes very thin sterilized plates of mica to avoid or correct postoperative nasal synechia. Its suppleness and its flexibility permits it to be readily insinuated between the raw surfaces, and it thus forms a thin partition which does not present the inconvenience of a foreign body, nor produce any secretion or granulation, and cicatrization is thus facilitated on both sides.

---

**A New Treatment for Paralysis of the Recurrent Nerve.**—BRÜNINGS claims (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911) to overcome the effects of the paralysis by stiffening the paralyzed vocal band artificially with hard paraffin injections. This he usually accomplishes in two sittings. In the first one he injects the middle, anterior, and posterior portions of the vocal band about midway of its transverse surface. Five to eight days later the intermediate portions of the vocal band are injected. In this way he succeeds in converting the flaccid vocal band into a stiffened structure in permanent position for phonation.

**Facial Paralysis following the Use of the Nasal Douche.**—LEBUT-BARBON reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 7 Livraison, 1912) a case of a man, aged thirty-nine years, who was in the habit of washing his nose every day for nasal catarrh. On one occasion this produced intense pain in the left ear, followed four or five days afterward by a facial paralysis which existed for six weeks and gradually subsided spontaneously.

**Laryngeal Paralysis as the First Symptom of a Cancer at the Base of the Skull.**—MAHU reports (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) this case in a very robust man, aged fifty-four years, and a great smoker, who consulted him for aphonia, pain in the temporomaxillary region, and a left recurrent paralysis, with very slight cervical adenitis. Eight days later inequality of pupils suggested neoplasm at the base of the brain, then tumefaction occurred rapidly, and finally an ulceration at the vault of the pharynx, with purulent discharge and invasion of the left nasal fossa and maxillary sinus. The recurrent paralysis had existed only fifteen days. The patient died cachectic at the end of four months after ineffective treatment with radiotherapy.

**Secondary Cancer of the Larynx.**—Secondary cancer of the larynx is very rare. A case has been reported by LANNOIS and MONTCHARMONT (*Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar.*, 6 Livraison, 1912) in which the patient succumbed two days after his entry to the hospital where he had been admitted with the diagnosis of cancer of the larynx at the level of the right arytenoid and the right aryteno-epiglottic fold. At the autopsy there was in addition, an epithelioma of the ectodermic type in the middle portion of the esophagus. Other cases on record have been traced as true metastases in cancer of the breast, of the rectum, and of the skin.

**Gastroscopy.**—In a demonstration on gastroscopy before the German Laryngological Association (*Verhandlungen des Vereins Deutscher Laryngologen*, 1911), ELSNER exhibited a gastroscope with an optical cystoscopic attachment which enables him to inspect the interior of the entire stomach within two or three minutes.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME  
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT;  
SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

**Pneumococcus Infection in Man and Animals.**—WADSWORTH (*Jour. Exp. Med.*, xvi, No. 1, July, 1912) publishes two interesting papers

giving results of experimentation directed to the possibility of a cure of pneumococcus infection. The author considers that we may liken lobar pneumonia in man directly to pneumococcus infection in animals. A rabbit is extremely susceptible, with production of a general systemic infection from which recovery may occur by crisis; the dog, on the other hand, tends to show local tissue reaction due to the fact that its protective mechanism is powerful, so that although there be characteristic lung lesions, crisis does not occur. Wadsworth is inclined to think that it is the bacteriemia rather than the lung lesion which accounts for many of the manifestations of the disease seen in man. The extensive lesion is an expression of the efficiency of the protective mechanism of the body, with the result that infectious agents in such lesions may actually disappear. Extensive lesions, however, are due at their inception to virulent pneumococci, and this virulence is a necessity before the systemic manifestations can occur. Immune sera are well-known to vary greatly in their curative value, although this does not necessarily mean that their protective action is slight. When animals are actively immunized, their immunity to culture filtrates is very definite, but injections with dead culture material are by no means so efficient as injections with virulent living cultures. In rabbits, treatment with such serum induces crisis and cure, but although virulent pneumococci show little reaction in the test-tube to a given serum, nevertheless subsequent infection by the special organism is an exception to the general rule. The pneumococcus toxins are presumably active only in the body tissues, and manifestations of the disease arise from this action. Immune sera can neutralize these poisons and terminate the symptoms of the disease, the pneumococci remaining as parasites to be destroyed in the ordinary course of events. This immunization may occur quickly and completely as in crisis, or in contrary manner, as in lysis. By analogy, Wadsworth considers that sera from animals highly immunized with living cultures of virulent organisms ought to cure the disease.

---

**Hemoglobinemia and Hemoglobinuria.**—PEARCE, AUSTIN, and EISENBREY (*Jour. Exp. Med.*, September, 1912, xvi, No. 3) give details of experiments with normal and splenectomized animals with regard to the excretion of hemoglobin. They find that there is a "threshold value" for the kidneys by which, when a concentration of 0.06 grams of hemoglobin per kilo of body weight is reached, the hemoglobin appears in the urine. The amount of hemoglobin per kilo of body weight which may exist without excess of bile pigments appearing in the urine, is about 0.22 grams, and this marks the "threshold value" of hemoglobin for the liver, although it is pointed out that the more slowly the hemoglobin is injected, the less likelihood is there of the appearance of choluria. When a relatively large amount of hemoglobin is injected intravenously, hemoglobinuria appears in a very few minutes; if a relatively small quantity be injected rapidly, it may appear with choluria; even moderately large amounts slowly injected may be eliminated without the occurrence of choluria. The absence of the spleen does not appear to affect the elimination of hemoglobin by the kidneys. Pearce, Austin and Eisenbrey's idea is

that hemoglobinuria does not occur until hemoglobinemia reaches the level of 0.06 gram per kilo body weight. When this amount is surpassed hemoglobinuria occurs, and when the concentration is less than this it ceases. The liver, however, and perhaps other tissues, take up hemoglobin as soon as it appears in the serum, and deal with it regardless of its excretion by the urine. The kidneys remove 17 to 36 per cent., and the liver takes the rest to be transformed into bile pigment. If the circulation be flooded with a large amount of hemoglobin absorbed rapidly, the bile pigments cannot be rapidly enough removed, and reabsorption into the blood occurs with the appearance of choluria. Pearce, Austin, and Eisenbrey would thus explain those cases in which hemolysis is accompanied by jaundice without hemoglobinuria; the liver removes the hemoglobin so rapidly that the minimum necessary for hemoglobinuria is not reached. Nevertheless, even under these circumstances a liver may absorb a large amount of hemoglobin so that bile formation is so excessive that jaundice appears. As a corollary to this, a very large amount of hemoglobin appears quickly in the urine until the excess has been removed, when it no longer appears, the slow elimination of the remainder by the liver causing the subsequent choluria. Experiments by Pearce, Austin, and Krumbharr with regard to splenectomy leads them to suppose that the spleen is essential for the breaking up of hemoglobin, or for the building up of its derivatives, and that there is an interrelation between the spleen and the blood-forming organisms, as well as between the spleen and other blood-disintegrating organisms. The bile-forming function of the liver is disturbed by splenectomy so that in the first four weeks after the operation, hemoglobinuria was not followed by jaundice, while after a period of three and a half months jaundice occasionally occurs, apparently indicating a rehabilitation of the function of the liver.

---

**Salvarsan and Sublimate.**—An account was recently given (*Jour. de Phys. et Path.*, July 15, 1912, xiv, No. 4) in which MOREL, MOURIQUAND, and POLICARD have made a comparison between the effects of toxic doses of salvarsan and of bichloride of mercury. Salvarsan has, relatively, a slight effect upon the kidney and a relatively marked effect upon the liver; about three times as much arsenic will lodge in the hepatic cells as will be found in the renal epithelium. As is well known, bichloride of mercury attacks the kidney with great avidity, so that the organ is rapidly damaged; on the contrary, its action upon the liver is relatively slow and slight, the action in each case bearing a direct relationship to the amount of the drug. It may be recalled that Oettinger and Fiessinger were enabled to examine a case of poisoning by intramuscular injection of mercury, and to discover 0.01 centigram of mercury for each 1000 gram of liver tissue, while three times as much was found per 1000 grams of kidney tissue.

---

**The Distribution of Iodine in Normal and in Syphilitic Tissue.**—The researches of O. LOEB (*Archiv. f. Exp. Path.*, 1912, lxix, 108) upon this subject support the belief that when iodid of potash is absorbed in health it does not remain in any demonstrable quantity in the

brain, the fat, or the bone marrow. It can be found in the liver, kidneys, lungs, the blood, and the thyroid glands. Disease in these and other tissues alters their adaptability to retain iodine, so that tuberculous or carcinomatous tissue contains more iodine than the same tissue in health. Secreting glands which are diseased by syphilis contain from three to six times as much as normal blood, and the less severe the syphilis, the greater the readiness of the tissue to hold iodine. In such tissues the iodine is in an organic combination, presumably an iodine and albumin compound being formed. It has doubtless been a puzzle to every reader to understand the action of so-called "alteratives;" it is, however, in tissue irritated by a virulent agent that these show their best powers, due perhaps to the readiness with which iodine forms (soluble?) combinations in such tissues. Certain it is that at times gummas or other proliferations of endothelial tissue seem to melt away under the action of iodine.

---

**The Parasitology of Trypanosomiasis.**—WOLBACH and BINGER (*Jour. of Med. Research*, September, 1912) have investigated the histological changes observed in trypanosomiasis. While their results show nothing remarkably new, they have examined with much care, the lesions set up by the presence of trypanosomes. As has been previously shown, these are decidedly of the nature of connective-tissue reaction to an irritant of low virulence. The essential change is proliferation of endothelial cells, and the activity of these cells, resulting from the presence of the parasites, causes the increase of large mononuclear cells which can be observed in the blood. Following the invasion of the tissue, there may be edema, there is constantly cell proliferation, fibrosis, and infiltration by plasma cells. The endothelial cells may block the vessels and undergo hyaline degeneration, after which fibrosis is seen to occur with occasional giant-cell formation. Granular leukocytes are conspicuously absent in the lesions, and when the parasites are engulfed it is in almost every case by the endothelial cells. Although lesions are to be found everywhere, the connective tissue structures are especially prone to be the seat of change, a case parallel to the changes observed in syphilis, although it must be noted that the trypanosome has little power to invade the skin. Wolbach and Binger have been able to observe the parasites setting up lesions in the central nervous system. From all the lesions observed, Wolbach and Binger deduce a very low degree of toxicity in the parasites, and the form of parasite which they consider most active in producing lesions in the flagellate.

---

**The Disinfection of Drinking Water by Chlorinated Lime.**—ANTONOWSKY (*Zeitschr. f. Hyg. u. Infekt.*, 1912, lxxii, Heft 3) investigated the possibilities of disinfecting water for drinking purposes by minimal amounts of chlorinated lime, and found that the method was a good adjuvant to the usual mechanical means. The efficient agent in the chemical is the acid, and a certain duration of time to allow its action is essential; if the time allowed be too short, the bacteria are not killed; and in the experiments in which the destruction of bacteria was incomplete, the virulence of those organisms that remained was

not affected in the slightest degree. The action of chlorinated lime can be nullified by the presence of sodium hypochlorite, and assisted by the presence of katalysing substances.

---

**The Experimentally Alcoholic Heart and Liver.**—BISCHOFF (*Zeitschr. f. Hyg. u. Infekt.*, 1912, lxxii, Heft 3) in dealing once more with this much-studied question, places the cardiac change in the most prominent place; true it is that central grouping of the fat occurs in the liver, but in rabbits the heart muscle changes are by far the more important. The site of predilection for the intracellular deposit of fat Bischoff states to be under the epicardium of the left ventricle toward the apex, as well as in the papillary muscles; the outer lamellæ of the right ventricle are also liable. The kidneys were not found to be markedly affected. The fat content measured from the dried substance of the heart showed in rabbits fed with alcohol a rise from 11 to 12 per cent; lecithin-content showed a considerable decrease, both absolute and relative; lecithin, which was nearly 60 per cent. of the total fat-content in the normal, became only 37 per cent. in the alcohol-fed animal, with a corresponding lessening in amount of cholesterin.

---

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.



# CONTENTS

## ORIGINAL ARTICLES

- Partial Gastrectomy in a Case of Multiple Carcinoma of the Stomach** . . . 781  
By JOHN H. GIBBON, M.D., Professor of Surgery in the Jefferson Medical College, Philadelphia.
- The Effects of Medicinal Doses of Aconite upon the Pulse-rate** . . . 788  
By R. D. RUDOLF, M.D. (Edin.), F.R.C.P., Professor of Therapeutics in the University of Toronto, and C. E. C. COLE, B.A., M.B. (Tor.), Demonstrator in Therapeutics, University of Toronto, Canada.
- Lupus Erythematosus and Raynaud's Disease** . . . 793  
By M. B. HARTZELL, M.D., LL.D., Professor of Dermatology in the University of Pennsylvania, Philadelphia.
- Some Features of the Gross Anatomy of the Spinal Cord and Nerve Roots, and Their Bearing on the Symptomatology and Surgical Treatment of Spinal Disease** . . . 799  
By CHARLES A. ELSBERG, M.D., Professor of Clinical Surgery in the University and Bellevue Hospital Medical College, New York.
- Bence-Jones Proteinuria: A Report of Four Cases, with Some Chemical and Biological Notes** . . . 803  
By THOMAS R. BOGGS, M.D., Associate Professor of Medicine, Johns Hopkins University; Physician in Chief, City Hospital at Bay View, and C. G. GUTHRIE, M.D., Instructor in Medicine in Charge of the Clinical Laboratory; Assistant Resident Physician, Johns Hopkins Hospital, Baltimore.
- Further Experiences with the Complement-fixation Test in the Diagnosis of Gonococcus Infections of the Genito-urinary Tract in the Male and Female** . . . 815  
By HANS J. SCHWARTZ, M.D., Instructor in Clinical Pathology and Clinical Instructor in Dermatology in Cornell University Medical School, New York, and ARCHIBALD McNEIL, M.D., Department of Health Research Laboratories, New York.
- Indicanuria** . . . 827  
By WILLIAM GERRY MORGAN, M.D., Professor of Gastro-enterology, Georgetown University, Washington, D. C.
- Adenocarcinoma of the Thyroid, with Metastasis to the Cervical Glands and Pituitary. A Contribution to the Pathology of Abnormal Fat Formation** . . . 834  
By D. J. MCCARTHY, M.D., Professor of Medical Jurisprudence, University of Pennsylvania, and HOWARD T. KARSNER, M.D., Assistant Professor of Experimental Medicine, Harvard University.
- Softening of the Spinal Cord in a Syphilitic after an Injection of Salvarsan** 848  
By LEO NEWMARK, M.D., San Francisco, Cal.

<b>Banti's Disease and Allied Conditions</b> . . . . .	856
By RICHARD STEIN, M.D., Visiting Physician to the German and the Lebanon Hospitals, New York.	
<b>Cases of Juvenile Psychasthenia: To Illustrate Successful Treatment</b> . . . . .	865
By TOM A. WILLIAMS, M.B., C.M. (Edin.), Corresponding Member, Societies of Neurology and Psychology of Paris, etc.; Neurologist to the Epiphany Dispensary, Washington, D. C.	
<b>The Incidence of Purpura in the Course of Chronic Pulmonary Tuberculosis</b> . . . . .	875
By JOHN M. CRUCE, A.B., M.D., Physician to the Henry Phipps Institute of the University of Pennsylvania, the White Haven Sanatorium, and to the Out-Patient Department of St. Agnes' Hospital; Instructor in Medicine in the University of Pennsylvania; Fellow of the College of Physicians of Philadelphia, and Member of the John Morgan Society.	

---

## REVIEWS

A Treatise on Diseases of the Hair. By George Thomas Jackson, M.D., and Charles Wood McMurtry, M.D. . . . .	885
Pharmacology and Therapeutics. By H. C. Wood, Jr., M.D. . . . .	886
Surgical After-treatment. By L. R. G. Crandon, M.D., and Albert Ehrenfried, M.D. . . . .	888
The Surgical Clinics of John B. Murphy, M.D. . . . .	889
The Practice of Medicine. A Manual for Students and Practitioners. By Hughes Dayton, M.D. . . . .	890
Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., assisted by Leighton F. Appleman, M.D. . . . .	890
The Pituitary Body and Its Disorders. Clinical States Produced by Disorders of the Hypophysis Cerebri. By Harvey Cushing, M.D. . . . .	891
Diseases of the Stomach with Especial Reference to Treatment. By Charles D. Aaron, Sc.D., M.D. . . . .	892
Primary Malignant Growths of the Lungs and Bronchi. By I. Adler, A.M., M.D. . . . .	893
The Principles of Anatomy. The Abdomen Proper Described and Illustrated by Text and Plates. By Wm. Cuthbert Morton, M.A., M.D. (Edin.) . . . . .	894
My Method of Preparing the Operative Field with Tincture of Iodine. By Kgl. Rat Dr. Antonio Grossich . . . . .	895
An Index of Treatment by Various Writers. Edited by Robert Hutchison, M.D., F.R.C.P., and H. Stansfield Collier, F.R.C.S. . . . .	896
The Skiagraphy of the Accessory Nasal Sinuses. By A. Logan Turner, M.D., F.R.C.S.E., F.R.S.E., and W. G. Porter, M.B., B.Sc., F.R.C.S.E. . . . .	897
Diagnose und Fehldiagnose von Gehirnerkrankungen aus der Papilla nervi optici. By Professor Dr. Fr. Salzer . . . . .	898

The Bacillus of Long Life. A Manual of the Preparation and Souring of Milk for Dietary Purposes, Together with an Historical Account of the Use of Fermented Milks, from the Earliest Times to the Present Day, and Their Wonderful Effect in the Prolonging of Human Existence. By Loudon M. Douglas, F.R.S.E. . . . .	898
Modern Microscopy. A Handbook for Beginners and Students. By M. I. Cross and Martin J. Cole . . . . .	899
Urologischer Jahresbericht. Edited by Dr. A. Kollmann and Dr. S. Jacoby . . . . .	900
Manual of Physiology. By H. Willoughby Lyle, M.D., B.S. (Lond.), F.R.C.S. (Eng.) . . . . .	900

## PROGRESS OF MEDICAL SCIENCE

### MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

Results of Antityphoid Vaccination in the Army in 1911, and Its Suitability for Use in Civil Communities . . . . .	901
Secondary Infections in Ulcerative Tuberculosis of the Lung . . . . .	901
Aortic Aneurysm of Rheumatic Origin . . . . .	902
Mechanical Production of Fever . . . . .	902
Experimental Digestive Leukocytosis . . . . .	903
Paroxysmal Ventricular Tachysystole of Psychic Origin . . . . .	903
The Chemistry of Tuberculous Sputa . . . . .	903
Adrenalin in Pathological Sera . . . . .	904
Malarial Pigment and the Malarial Paroxysm . . . . .	904
Albuminuria and Cylindruria . . . . .	905

### SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

The Influence of an Aseptic Serous Inflammation upon the Dissolution of Catgut . . . . .	906
An Experimental Contribution Concerning the Formation of Bone from the Injection or Implantation of Periosteum Emulsion . . . . .	906
Small Plastic Operations on the Fingers and Hands . . . . .	907
The Clinical Utilization of the Coagulation Time of the Blood in Jaundice . . . . .	907
The Surgery of the Deep Pelvic Lymph Nodes . . . . .	908
Statistical Contribution Concerning the Result of the Wilms Method of Treating the Stump in Resection of the Stomach . . . . .	909
A Study of Vesico-intestinal Fistulæ . . . . .	909
Treatment of Dislocation of the Head of the Radius Complicated by Fracture of the Ulna . . . . .	910

**THERAPEUTICS**

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

The Treatment of Syphilis with Neosalvarsan . . . . .	911
Experiences with Neosalvarsan . . . . .	911
The Treatment of Gout with Atophan . . . . .	911
The Treatment of Diphtheria Carriers by Overriding with Staphylococcus Aureus . . . . .	911
Vaccination for Typhoid by Living Sensibilized Bacilli Typhosi . . . . .	912
Hexamethylenamin in the Treatment of Systemic Infections, with a Special Emphasis upon Its Use as a Prophylactic . . . . .	913
The Crotalin Treatment of Epilepsy . . . . .	914
Further Experiences of the Specific Curative Action in Amebic Dysentery of Hypodermic Injections of Soluble Salts of Emetin . . . . .	915

**PEDIATRICS**

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

Serous Meningitis and Associated Conditions in Childhood . . . . .	915
Icterus Simplex in Childhood . . . . .	916
The Practical Significance of Uniformly Deep Rectal Temperature Measurements in a Child . . . . .	917
The Diagnosis of Tuberculosis of the Lungs in Children . . . . .	918

**OBSTETRICS**

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

The Treatment of Ectopic Gestation . . . . .	918
Normal Human Blood Serum in the Disorders of the Newborn . . . . .	920
Ocular Lesions in the Newborn . . . . .	920

**GYNECOLOGY**

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Vaccine Diagnosis of Gonorrhea . . . . .	922
Treatment of Injured Ureter by Appendiceal Implantation . . . . .	923
Normal and Pathological Anatomy of the Endometrium . . . . .	923
Treatment of Incontinence of Urine in Women . . . . .	924

**DERMATOLOGY**

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D., AND MILTON B. HARTZELL, M.D.

Some Physiotherapeutic Methods in Dermatology . . . . .	925
New Method of Removing Superfluous Hairs . . . . .	925
Treatment of Itching Skin Diseases with Normal Human Serum . . . . .	925
A Useful Formula for the Widespread Tinea Tonsurans . . . . .	926
Pemphigus Foliaceus . . . . .	926
Concerning the So-called Lichen Albus of Zumbusch . . . . .	926

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

DECEMBER, 1912

---

ORIGINAL ARTICLES

**PARTIAL GASTRECTOMY IN A CASE OF MULTIPLE  
CARCINOMA OF THE STOMACH.**

BY JOHN H. GIBBON, M.D.,

PROFESSOR OF SURGERY IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

INSTANCES of multiple primary malignant growths are sufficiently rare to warrant their publication. The following case of multiple primary carcinoma of the stomach is not altogether unique, but the recording of similar conditions has been infrequent.

H. K., aged forty-eight years, was sent into my service at the Jefferson Hospital by Dr. O. L. Wingate, January 4, 1912, and gave the following history: His family history was absolutely negative, his previous personal history was also negative; he had used beer, coffee, tea, and tobacco in moderation; he had always enjoyed good health and considered himself perfectly well until June, 1911, when he first developed gastric symptoms. At that time he was suddenly seized with a vomiting attack on the street, and says that the vomited material was black, and that he thought it contained blood. Repeated similar attacks occurred through the summer, and he rapidly lost weight and color. In the fall, under treatment, he improved, vomiting ceased, and he regained some weight and color. During the two months previous to admission the vomiting returned, and there was again rapid loss of weight and color. In the four weeks prior to admission he had lost twelve pounds in weight. The interesting point in his history, in view of the subsequent findings, is that he never had any pain or symptoms of indigestion, and the slight discomfort which he felt showed no

regularity as to the time of its occurrence. His chief complaint was vomiting, which did not occur every day, but he often vomited in the evening the food which he ate at breakfast. He thought that he had vomited practically all of the food taken during the few days previous to admission. He also complained of weakness and of tiring easily.

Examination showed a thin, very pale individual of distinctly cachectic appearance. Palpation of the abdomen revealed no tenderness, rigidity, or tumor. The blood examination was: Hemoglobin, 44 per cent.; red cells, 3,140,000; leukocytes, 12,000; color index, 0.7. The gastric analysis was: Free hydrochloric acid absent; total acids, 0.0584; combined acids, 0.02185; no lactic acid; no bile; considerable blood; a few Oppler-Boas bacilli; a few yeasts; a few epithelial cells. A diagnosis of probable gastric cancer was made, and the patient was sent to Dr. Manges for x-ray examination. The plates showed marked irregularity in the outline at about the middle of the greater curvature and again near the pylorus in the greater curvature. The motility of the stomach was considerably interfered with, but Dr. Manges did not think that there was an obstruction of the pylorus; his interpretation of the plates was that the condition was malignant and that there were two distinct lesions.

OPERATION. On January 27, 1912, under chloride of ethyl-ether anesthesia, preceded by morphine and atropine, the abdomen was opened through the left rectus, and at once a large round mass at about the middle of the greater curvature was found involving both the anterior and posterior walls. The mass was densely hard, and there were small nodules beyond it; the gastrocolic omentum was puckered and attached to the growth. About an inch from the pylorus, on the greater curvature, was another hard mass, with an excavated centre, which could be easily felt through the anterior wall. The whole stomach was freely movable; there was no pyloric obstruction; no adhesion to the pancreas; no marked enlargement of the glands. The case seemed a good one for resection of the stomach, and I thought that there would be enough of the organ left for a gastrojejunostomy. The blood supply of the area to be removed was first tied off, a ligature placed about the duodenum, and a clamp placed obliquely across the stomach from a point well above the larger growth to the cardiac end of the lesser curvature. The portion of the stomach included between the ligature and the clamp was then excised; the remaining pouch of the stomach was closed with two continuous catgut sutures and inverted with a continuous suture of linen thread. As the ligature around the duodenum did not completely close it, the cut end of this bowel was closed and inverted. I was surprised to find that the larger growth was adherent to the mesocolon, and I feared at first that the transverse colon itself was involved in the growth. I

found, however, that I could trim away the adherent peritoneum without opening the bowel. The jejunum was then brought up through an opening in the mesocolon and attached to the posterior wall of the cardiac end of the stomach by catgut and linen sutures. The patient lost little blood during the operation, which occupied about an hour, and at its conclusion his pulse was 86.

The patient's convalescence was perfectly satisfactory excepting that he had a slight infection of his wound, which necessitated his remaining in bed longer than usual. He was discharged from the hospital on March 7, 1912. I saw him last on March 30, when he told me that he was able to eat all kinds of food and had no discomfort whatever. In the three weeks which had elapsed since his discharge he had gained twelve pounds. He was still pale, but his color was much better than before operation, and although I hesitated to prognosticate a cure, I felt confident further improvement would take place.

July 23, 1912: The patient died on June 19 of general debility, but without the recurrence of any gastric symptoms whatever. His only complaint was weakness in the legs, and it was thought for a time that he might have a spinal metastasis, but this could not be definitely determined. He did not die in the hospital, and no autopsy was made.

As the principal interest in this case centres in the character of the growths found, I am including a full pathological report from the laboratories of the Jefferson Hospital.

"PATHOLOGICAL REPORT, January 27, 1912. Patient H. K. Specimen, stomach. The specimen is an irregular portion of stomach wall, measuring 15 cm. in length and varying in width from 13 cm. at the broader to 7.5 cm. at the narrower end.

"The mucous surface bears two ulcers. The larger extends to within 1 cm. of the broader extremity. It is oval in outline, being 7.5 cm. long and 6 cm. wide. A peripheral zone 1.5 cm. wide is elevated from 0.5 to 1 cm. above the surface of the stomach. The surface of this raised margin is quite uneven, and has many reddish areas where the mucosa is lacking, the latter for a large part of the circumference forming only the outer wall of the elevated portion and not covering its surface.

"Internally the elevated zone dips down abruptly to the floor of the ulcer proper, which is 3 by 3.5 cm. The floor is fairly smooth and appears to be formed by the muscle coat, although this cannot be stated with certainty. Near one margin of the depression is an almost circular area 1 cm. in diameter that is much deeper than the remainder. The floor of this small area is formed by the inner surface of a grayish nodule 2 cm. in length and 1 cm. in height that is attached to the peritoneal surface of the stomach; around the nodule is a narrow irregular zone of infiltration of the peritoneum that is but slightly elevated. This nodule is quite readily separated

from a part of its attachment to the tissue surrounding the ulcer, this separation causing the appearance of an opening into the latter; apparently the escape of stomach content had been prevented only by this adherent mass, the stomach wall having a complete circular perforation 1 cm. in diameter.

"The smaller ulcer is toward the narrow end of the specimen and 1.5 cm. from the border of the large one, with which it has no demonstrable connection, either superficial or deep. It is 3.5 by 5 cm. in size, the peripheral portion being elevated as in the larger one. This elevated part varies from 0.8 to 1.5 cm. in width, and is covered by mucosa except for a few points along the narrower portion. The depressed portion or ulcer proper is 2 cm. in diameter, with a fairly smooth, grayish floor, probably formed by the muscle coat of the stomach. The peritoneal coat is slightly elevated and thickened over the area corresponding to this lesion.



FIG. 1.—Portion of stomach wall, showing the larger and smaller ulcers.

"The gastric mucosa not involved by the ulcers is rather smooth, grayish-red in color, and is markedly corrugated, especially in the vicinity of the ulcerated areas. Incision of the raised margins of the ulcers encounters decided resistance, and the cut surfaces are somewhat granular, grayish-yellow in color, and quite uniform in texture.

"Small portions of each mass were fixed in alcoholic corrosive sublimate, cleared in cedar oil, embedded in paraffin, sectioned, and the sections stained with hematoxylin, eosin, and Van Gieson's mixture.



"Histology: Sections from the margin of the smaller of the two ulcers possess a partial border of gastric mucosa, which for the greater part shows but little change other than moderate infiltration by small round cells. In the depths this cellular infiltration is more prominent, and there is a moderate increase of intertubular connective tissue. Immediately below this is a rather abrupt transition to a newgrowth which has partly or entirely replaced the muscularis mucosæ and forms the remainder of the sections. This new growth is made up of tubules, very irregular in size and shape, which are separated by bands of connective-tissue stroma that in areas is well marked, in others less prominent. The stroma is possibly residual submucosa (from its position), or is new tissue developed as a part of the growth. The tubules are lined by columnar epithelial cells, mostly in a single layer, but in some tubules stratified. These cells are placed directly upon the fibrous stroma. Some of the tubules are partly filled by granular debris or desquamated and degenerating tumor cells. The stroma shows but little cellular infiltration.

"Sections from the wall of the larger ulcer also show a partial boundary of gastric mucosa. In areas the tubules at about their midpoint gradually merge into a structureless mass of rounded or polygonal cells which extend to, partly replace, and continue beyond the muscularis mucosæ as the remainder of the section. There is in many areas no definite stroma, in this mass of cells forming the newgrowth, connective tissue being very scanty. At each boundary of this area of transition of mucosa into the tumor, the latter extends below the muscularis without involving the overlying mucosa, the contrast between the structure of the two being very striking.

"Diagnosis: Both ulcers show carcinoma, which in each is in direct relation with the gastric mucosa. The structure of each, as above described, appears to justify the diagnosis of adenocarcinoma of the smaller ulcer and medullary carcinoma of the larger. In addition there is anatomical perforation of the larger ulcer, the opening being blocked by a mass of adherent newgrowth, presumably in a perigastric lymph node."

Dr. Despard and I have searched the literature dealing with multiple malignant growths, and one of the best accounts that we have been able to find is in Fenwick's<sup>1</sup> work.

Fenwick studied 1850 cases of cancer of the stomach, and in 54 or 2.9 per cent. multiple tumors were found, in three-fifths of these 54 cases, however, the tumors occupied corresponding spots on the anterior and posterior walls, and one showed a later development of the same type of cancer as the other. These were, in all likelihood, instances of transference by contact. Thus in about 1

<sup>1</sup> Cancer and Tumors of the Stomach.

per cent. there was no possibility of multiplication by contact, but in a number of these cases the growths were of exactly the same



FIG. 2.—Photomicrograph of section of smaller growth.



FIG. 3.—Photomicrograph of section of larger growth.

type and consequently can hardly be described as instances of multiple primary cancer of the stomach, a rare condition.

One of Fenwick's own cases presented a soft spheroidal-cell cancer of the cardia and a cylindrical-cell cancer of the pylorus. Several similar cases have also been collected from the literature by Fenwick.

D. D. Stewart,<sup>2</sup> reports a case operated upon by Dr. W. W. Keen, in which there were two isolated carcinomatous ulcers of the stomach: one was astride the lesser curvature of the stomach, and the other astride the greater curvature. The stomach in this case was removed post mortem, and a photograph of the specimen accompanies the report. Dr. A. O. J. Kelly examined the specimen and diagnosed the condition as adenocarcinoma.

In Osler and McCrae's work on *Carcinoma of the Stomach* a case is reported of multiple submucous carcinoma of the stomach found at autopsy. The largest of the growths in this case was polypoid in character. The other growths were similar but smaller. From the histological character of the different growths Dr. Welch regarded the case as an instance of multiple primary carcinoma of the stomach.

Instances of multiple primary carcinoma occurring in different organs is more frequent than the occurrence of the condition in the same organ. Warthin<sup>3</sup> reports 2 cases of multiple cancer found post mortem. In the first there was an adenocarcinoma of the ovary and a colloid carcinoma of the gall-bladder. In the second case there was an adenocarcinoma of the sigmoid and an adenocarcinoma of the gall-bladder, each growth having started in a polyp and being of different anatomical character. In both of these cases stones were present in the gall-bladder.

Fenwick reports a case of spheroidal-cell carcinoma of the pylorus and a cylindrical-cell epithelioma of the rectum.

Albert Bauer, in an interesting inaugural address (Kiel, 1907) discusses at length the question of multiple primary carcinoma, and reports 3 personal cases. The first is that of "adenoma malignum" of the greater curvature of the stomach and "adenocarcinoma" of the pylorus, with glandular metastases from the latter. The second case showed an epithelioma of the esophagus, near the bifurcation of the trachea, and an adenocarcinoma of the stomach. The third case was one of squamous-cell epithelioma of the penis and adenocarcinoma of the stomach.

When two cancers of the same structure are found in the same organ the occurrence may usually be attributed to transference by contact or to autoinfection. It may be that the latter explanation would apply to my own case. The clinical history does not

<sup>2</sup> AMER. JOUR. MED. SCI., November, 1898.

<sup>3</sup> Jour. Amer. Med. Assoc., May 6, 1899.

bear out the fact that we have a malignant change taking place simultaneously in two ulcers of the stomach. The patient was an intelligent man, and told me repeatedly that he never had any gastric symptoms until six or seven months before his operation.

## THE EFFECTS OF MEDICINAL DOSES OF ACONITE UPON THE PULSE RATE.

BY R. D. RUDOLF, M.D., (EDIN.), F.R.C.P.,

PROFESSOR OF THERAPEUTICS IN THE UNIVERSITY OF TORONTO,

AND

C. E. C. COLE, B.A., M.B., (TOR.),

DEMONSTRATOR IN THERAPEUTICS IN THE UNIVERSITY OF TORONTO, CANADA.

THE use of aconite as a medicine seems to date from 1762, when Baron Störck introduced the drug to practice. But aconite has been used by the laity from time immemorial, and few drugs have had a more varied history. Störck recommended the preparation as a diaphoretic and diuretic, and employed it in chronic rheumatism, gout, paralysis, phthisis, and a great variety of diseases. It was eagerly taken up by the profession, and for some years was enormously used, and then fell into disuse. In 1796 Hahnemann experimented with it, and recommended it in inflammatory fevers, where the allopathics would bleed. In 1835 M. Lombard, of Geneva, advocated its use as an anodyne and antiphlogistic in acute rheumatism and other acute local inflammations. "Under doses varying from  $\frac{1}{2}$  grain to 8 grains every two, four, or six hours the severest attacks of febrile rheumatism yielded in the course of two, four, or six days; and even protracted cases of subacute rheumatism were often cured. The relief of pain and abatement of fever commenced in a few hours, without any critical evacuation by the bowels, skin, or kidneys" (Christison<sup>1</sup>).

It appears to have been Alexander Fleming who first drew attention to the action of the drug in slowing the heart's beats. In 1845 he wrote a thesis upon the drug and showed how it slowed the heart's action. He described four stages, according to the amount given. After 5 minims of the tincture the heart slowed; the pulse, some four hours after the administration, would have fallen some eight beats. If a second dose were then given, or 10 drops had been given at first, the pulse would fall another eight beats and become weaker, but still regular. If two hours later 5 drops were again given the pulse would fall to perhaps half of its normal rate, but

<sup>1</sup> Dispensatory, 1848, p. 56.

still remain regular. In the fourth degree, after the taking of another dose of 5 drops, the pulse would become weak and irregular, and if the action of the drug were carried to a fatal extent the pulse would become gradually imperceptible. These results seem to be remarkable until we realize that Fleming used a tincture which was some six times as strong as the U. S. P. tincture, and therefore about twelve times the strength of the B. P. tincture. He made it by passing 24 fluidounces of rectified spirit through 16 ounces of powdered aconite root, while the U. S. P. tincture is 1 in 10 and the B. P. tincture about 1 in 20. Thus Fleming used doses corresponding to  $\frac{1}{2}$  to 1 dram of the U. S. P. tincture, the maximum official dose of which is 15 minims, and for repeated doses 1 to 5 minims.

Ringer and Murrell next introduced the employment of small but frequently repeated doses, and under the influence of the former's book, passing through its many editions, this method of using the drug has become widespread, although of late years one does not hear so much of it. Ringer especially recommended its use in the treatment of inflammations accompanied by fever, and indeed said: "In the treatment of inflammations the thermometer and aconite should go hand in hand."<sup>2</sup> He gave  $\frac{1}{2}$  to 1 drop (of the B. P. tincture) every ten minutes for two hours and then every hour, and such is the usual suggestion that echoes through most of the text-books to the present day. Under such treatment the pulse is believed to become slow, the fever to lessen, and the skin to become moist.

But in the doses recommended in the pharmacopœias, and still less in those suggested by Ringer and Murrell, the pulse does not seem, according to our observations, to be at all affected. With any other effects of the drug we are not here concerned.

One fact that stands out with great clearness is that aconite in sufficient amounts is a violent poison, acting powerfully upon the circulation, and finally killing by paralyzing the respiratory centre. Thus we found that 1 c.c. of a solution of the crystalline aconitine of 0.0225 per cent. (the strength of the B. P. tincture) killed a guinea-pig in a few minutes. In less powerful but still large doses it has a marked action on the heart, slowing it, chiefly through the vagus. S. A. Matthews<sup>3</sup> has recently shown how aconitine slows the heart of the dog and lowers the blood pressure. But he used  $\frac{1}{16}$  mg. of aconitine (Boehringer's) injected and repeated in twenty minutes, which is an enormous dose. He concludes that the action consists in "a stimulation of the inhibitory mechanism of the heart, especially of the centres in the medulla. Next an increase in the irritability of the muscle of the auricle and ventricle." He says that "the first of these is the only effect seen in the therapeutic use of

<sup>2</sup> Handbook of Therapeutics, p. 343.

<sup>3</sup> Jour. Exper. Med., September, 1897.

the drug, and aconitine may, therefore, be considered to be indicated when it is desirable to stimulate the inhibitory centre without action on the heart muscle." This, of course, refers to very large doses, but, as already said, in doses such as are recommended in the pharmacopœias, and especially in the fractional doses introduced by Ringer and Murrell, the effect upon the circulation is *nil* according to our findings. These negative results may have been due to either of two causes: (1) Either the tincture used in the experiments was weak or inert, or (2) the doses were too small to have any appreciable effect.

F. W. Price found that several, in fact all, of the samples that he obtained from reputable druggists in England were inert when tested in Professor Cushny's laboratory. Next he obtained an active *aconitine* from this laboratory, and still found that the drug, even in doses far larger than those recommended in the British Pharmacopœia, had no effect upon the pulse rate, and, rather as a side issue, had no influence upon the blood pressure. These results were embodied in a paper which he presented before the Royal Society of Medicine in 1911.<sup>4</sup> During the past year the writers have tested the drug in many cases, as regards the effects upon the pulse rate, always using medicinal doses, and this paper gives the results of their work.

To commence with, we used the ordinary B. P. tincture, which happened to be in the Toronto General Hospital, and which had been obtained, as we afterward found, from three reputable firms of wholesale druggists. The pulse rate was usually taken for hours before and for hours after the administration, and in many cases the blood pressure was also measured, but no effect upon the circulation was detected. Often considerable fluctuations were seen, but it was found that these were mere coincidences and were just as apt to occur without the aconite. After finding no effects from the administration of the hospital tinctures we wrote to a well-known drug firm and they kindly forwarded a quantity of B. P. tincture "which has been tested both physiologically and by assay in the laboratory, and which we guarantee is of B. P. strength." Most of our experiments were done with this tincture, and were still negative. Then we asked Dr. V. E. Henderson, associate professor in charge of the pharmacological department of the University of Toronto, to test this tincture, and he reported it as very weak. The bottle had stood in a room at about 60° F. for some three months before he tested it, and probably had depreciated since we first obtained it, but our experiments were chiefly done soon after we got it. Next the same firm kindly sent us some pure crystalline aconitine, which Dr. Sharpe, of the pharmacological department, found by experiments on animals to be of full activity.

He was good enough to make for us a solution of it corresponding in strength to the B. P. tincture, namely 0.0225 per cent. (1 c.c. of this solution killed a guinea-pig in a few minutes), and we continued our experiments with this solution, still with negative results.

Our experiments were done upon two classes of patients: (1) Those with normal pulses, and (2) those with fast pulses. Some of the latter had fever and some had normal temperatures. In none of them (55 in all) was any decided effect upon the pulse rate observed. Occasionally the pulse would be found to be slow after the taking of the drug, but when the pulse was watched for hours before and after the administration it was seen that such fluctuations occurred without any aconite. The psychic effect of the administration, with the frequent taking of the pulse, must be taken into account. In one case of persistent tachycardia, following typhoid fever, the pulse dropped some forty beats for twelve hours after small repeated doses were given, which looked like a marked effect; but when the experiment was repeated upon the same individual under exactly the same conditions no such result, or rather sequence, occurred.

It appears from both Dr. Price's findings and our own that the tincture of aconite on the market is usually inert. We have discussed this matter with Dr. McGill, chief analyst to the Inland Revenue Department of Canada, and he hopes soon to examine samples from various parts of the Dominion, and the results will be interesting. The difficulties of testing the drug, however, are great. The aconite root contains at least three active principles—*aconitine*, *aconine*, and *benzaconine*—and, although it is an easy matter to assay the total alkaloids, it is very difficult to find the proportion of aconitine, and yet it is upon this alkaloid that nearly the entire action of the root depends. A simpler test, and one which is chiefly employed by the manufacturing houses, is the "Squibb test." This depends upon the fact that aconitine, and it only, produces, when applied to the tongue in great dilution, a tingling there. A solution of 1 in 500,000 of aconitine will give this reaction. Similarly a solution of 1 in 70 of the American tincture or 1 in 35 of the B. P. preparation should act in the same way. A dram of the dilution is held in the anterior part of the mouth for exactly one minute and is then discharged. A distinct tingling should be perceived within ten to fifteen minutes. Mr. F. O. Taylor,<sup>5</sup> who has written extensively upon the tests for aconite, and gives a very complete bibliography, believes that this is the best practical test that we possess. None of the tinctures that we procured gave this reaction, but the solution of crystalline aconitine which was of the strength that the tincture should be, and was then diluted as described, gave it very distinctly. It is interesting, however,

<sup>5</sup> Jour. Industrial and Engineering Chemistry, August, 1909.

to note that this same solution would not give the Squibb test three months later until diluted four times less than before, which shows how aconite depreciates with keeping.

Even when the drug is active, small doses seem to have no effect upon the pulse rate. How then may we explain the reports to the opposite effect which teem in medical literature, and which support the advice found in nearly every text-book on therapeutics and medicine. To our minds it is another example of the *post ergo propter* fallacy, which fallacy is so often seen in medicine, and which has so frequently been responsible for many findings which further trial has shown to be without foundation—something is given and the patient improves: *ergo*, the improvement is due to the something given.

The examples of marked and even dangerous effects following small medicinal doses of aconite, which are occasionally chronicled, can only be due to one of two things: (1) Either there has been some mistake in the dispensing or administration of the drug, so that the patient has received far more than was intended, or (2) an idiosyncrasy must have existed so that toxic effects were obtained from a dose which ordinarily has no effect. For example, Woodbury<sup>6</sup> records a case of nearly fatal poisoning from 3 drops of the tincture. No doubt, as Shoemaker<sup>7</sup> says, "The toxic dose and the susceptibility to aconite both vary greatly in different subjects."

It can truly be said that the theme of this paper is destructive rather than constructive, but surely the subject of therapeutics almost more than any other part of the domain of medicine requires destructive criticism in order that we may clear away the chaff and thus make more clear the valuable parts that remain. The pharmacopœias of old contained many weird substances, such as human urine, which were gravely prescribed by earnest men, and good followed; and yet we do not believe nowadays that that good resulted from the remedy used. And the pharmacopœias of today contain many substances which might well be left out, and we believe that aconite, certainly in the doses recommended, is one of these.

As already said, aconite, when given in massive doses, is an extremely powerful body, and it may be of great value where it is desired to slow the pulse or obtain some of its other effects; but this paper is not dealing with such uses of the drug at all.

<sup>6</sup> Proc. Coll. of Phys. of Philadelphia, 3d series, x, 450.

<sup>7</sup> Mat. Medica and Therap., p. 151.



Dosage of B. P. tincture.	Condition of patients.	Age.	Effects on pulse rate.
One minim every ten or fifteen minutes for eight to ten doses.	Eight convalescents with normal pulse rates.	..	Nil.
	Eight convalescents with fast pulses.	..	Nil.
	Post-typhoid tachycardia.	25	Nil.
	Post-typhoid neuritis.	45	Nil.
	Two healthy orderlies.	..	Nil.
	Tuberculous knee.	20	Nil.
	Typhoid fever.	22	Nil.
Two minims every ten to fifteen minutes for eight to ten doses.	Acute tonsillitis.	23	Nil.
	Hysterical vomiting.	21	Nil.
	Cholecystitis.	50	Nil.
Three minims every ten to fifteen minutes for eight to ten doses.	Convalescent typhoid.	25	Nil.
	Gallstones.	28	Nil.
	Rheumatoid arthritis.	23	Nil.
	Streptococcic septicemia.	24	Nil.
	Pleuropneumonia.	55	Nil.
	Septicemia.	24	Nil.
Four minims every ten minutes for eight doses.	Convalescent pleurisy.	28	Nil.
	Pleuropneumonia.	25	Nil.
	Pleuropneumonia, repeated.	..	Nil.
Four and one-half minims every ten to fifteen minutes for eight to ten doses.	Phthisis pulmonalis.	30	Nil.
	Convalescent typhoid.	25	Nil.
	Rheumatic arthritis.	60	Nil.
	Hysteria.	22	Nil.
Two minims every hour for four doses.	Convalescent typhoid.	25	Nil.
Three minims every hour for ten doses.	Convalescent typhoid.	25	Nil.
	Tuberculosis.	30	Nil.
	Mitral stenosis.	22	Nil.
	Gallstones.	22	Nil.
	Arthritis deformans.	21	Nil.
Four and one-half minims every thirty minutes for ten doses.	Tuberculosis.	30	Nil.
Six minims every hour for ten doses.	Post-typhoid neuritis.	45	Nil.
	Arthritis deformans.	22	Nil.
Ten minims every hour for ten doses.	Exophthalmic goitre.	18	Nil.
	Splenomyelogenous leukemia.	45	Nil.
	Chronic rheumatism.	25	Nil.
One dose of fifteen minims.	Neurasthenia.	21	Nil.
	Rheumatoid arthritis.	25	Nil.

## LUPUS ERYTHEMATOSUS AND RAYNAUD'S DISEASE.

BY M. B. HARTZELL, M.D., LL.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

M. C., a young unmarried woman, aged twenty-four years, first came under observation at the Skin Dispensary of the University Hospital, Philadelphia, in December, 1908, where she

had come for advice concerning a disease of the skin affecting principally the hands and feet, more especially the fingers and toes. At this time the fingers, which were apparently somewhat atrophied, were a deep bluish-red color with a number of small pearly white, stippled, scar-like patches scattered over their palmar surface, and a small, thickly crusted ulcer on the palmar surface of the second phalanx of the left thumb, and one on the tip of the left index finger. The palms were also affected, but to a much less degree than the fingers, showing only two or three small scar-like areas in each, and a single small oval ulcer on the ulnar side of the left one. The toes of both feet were quite livid, the discoloration being patchy on the smaller ones, and there were a considerable number of small scar-like lesions like those on the fingers. In addition to these lesions on the fingers and toes there was a very ill-defined, rather dusky patch on the right ear. Tactile sensation in the fingers was somewhat impaired, and the patient occasionally complained of a numb feeling in the hands as if, to quote her own words, "a rubber band was around the wrist." She suffered much from a most distressing burning and aching of the fingers and toes which was not continuous, but came on at irregular intervals, being especially severe just preceding the formation of the ulcers. The disease had lasted two years and had finally compelled the patient to give up her occupation, which was that of a saleswoman.

During the next few months there was but little change in the condition of the fingers. It was noted that the lividity varied much from time to time and was apt to occur paroxysmally; on one occasion the patient stated that while on her way to the dispensary the right ring-finger became "quite black" for a short time. It was noted, too, that the tips of one or more of the fingers became dead-white and waxy looking at times and remained so for a period varying from a few hours to two or three days, this condition being occasionally followed by the appearance of small blebs in the same situation and later by superficial eschars. Small ulcers similar to those upon the fingers occurred upon the toes, but apparently less frequently.

In May, 1909, a small, oval, violaceous, slightly scaly patch was observed on each upper lid near the inner canthus, which presented the features of an ordinary lupus erythematosus, these with the faint patch on the ear already referred to being the only evidence of cutaneous disease noted elsewhere than upon the extremities throughout the entire period of observation. During the summer months of this year the condition of the hands was somewhat improved; they were less discolored and there was much less pain, except for a period of a week or two in June when there was a rather severe inflammation with suppuration about the roots of the nails. With the advent of colder weather, however,

about the end of October, the fingers became much redder, there was a decided increase in pain, and a considerable number of small flaccid blebs appeared upon the hands, palms as well as fingers. According to the statement of the patient there was always a marked increase in all the symptoms with the appearance of cold weather, but this was the severest attack she had ever had. Throughout the winter of 1909-1910 small pea-sized ulcers continued to appear at irregular intervals upon the hands and toes, usually preceded by small blebs, the patient complaining much of pain while these were forming. About the end of March, 1910, she ceased attendance at the dispensary, but it was learned subsequently from a sister that the condition of the hands remained much the same during the next year. She then had a severe attack of facial erysipelas complicated by malignant endocarditis which terminated fatally.

To recapitulate the salient features of this unusual case, there were (1) certain vascular phenomena, such as cyanosis of the extremities alternating with extreme local ischemia frequently followed by the formation of blebs and superficial necrosis of the ischemic areas, accompanied by severe burning and aching, aggravated by cold, symptoms characteristic of Raynaud's disease; and (2) violaceous patches on the ear, eyelids, and toes, with numerous small, bluish-white, atrophic areas on the hands and feet, lesions characteristic of erythematous lupus.

The association of erythematous lupus with certain vascular symptoms, such as cyanosis of the hands and feet, the ears, and nose, especially noticeable in cold weather has frequently been noted by dermatologists, and special names have been employed to designate the forms of the disease in which such symptoms are a prominent feature. Practically no mention, however, is made in text-books on diseases of the skin of cases presenting the very marked vasomotor symptoms described in some detail in the case just reported, although I have found an unexpected and relatively considerable number of cases resembling it more or less closely, scattered throughout the journals devoted to dermatology. A brief review of the cases which I have collected will not only serve to illustrate the character of the relationship between these two maladies, but will demonstrate, as I believe, that the relationship is intimate and real and not accidental.

CASE I.—A woman, aged thirty-five years, who suffered from a joint affection which was regarded as chronic rheumatism, had numerous small ulcerations on the face, forearms, and feet which left conspicuous white scars. The skin of the face was stiff and wooden, like morphea. The fingers became white and cold, and subsequently dusky, upon the slightest exposure, and many of the nails became inflamed and suppurated at their roots. Upon the abdomen and over the front of both thighs were erythematous

patches presenting the characteristics of erythematous lupus. The case was regarded by Mr. Hutchinson,<sup>1</sup> who reported it, as a mixed one of erythematous lupus and Raynaud's disease.

CASE II.—An unmarried woman, aged nineteen years, was the subject of a peculiar vesicating erythema of both cheeks, which was looked upon by Mr. Hutchinson<sup>2</sup> as most likely an irregular form of lupus erythematosus. In addition to this affection of the cheeks the fingers were swollen, dusky, and cold, with deep-seated vesicles along the sides; the ears were swollen in like manner, and the nose was cyanotic and cold. Puffy swellings developed on the extremities in the course of a few hours, then rapidly disappeared, leaving greenish-yellow, bruise-like stains.

CASE III.—A woman, aged twenty-three years, had at first "typical Raynaud's disease," resulting in gangrene of the tips of some of the fingers, and this was followed one year later by a "bat's wing" erythematous lupus of the face. Two years later the hands presented a characteristic sclerodactylia, and there was likewise a scleroderma of the face (Pringle).<sup>3</sup>

CASE IV.—A delicate girl, aged seventeen years, had an accurately symmetrical "bat's wing" patch on the face containing numerous dilated sebaceous-gland ducts. The hands were blue and cold, and were covered with livid erythematous patches, as also were the toes. The tips of both little fingers were gangrenous, while gangrene of several others seemed to be impending; the disease was accompanied by great pain. The case was shown as one of lupus erythematosus and Raynaud's disease.<sup>4</sup>

CASE V.—A neurotic woman, aged forty-four years, had attacks of localized syncope alternating with local asphyxia of the extremities, particularly of the hands. The nutrition of the fingers was much impaired; they were stumpy and atrophied, but gangrene had not occurred. Five years later erythematous lupus occurred in the temporal region and on the scalp. This patient suffered much from cold.<sup>5</sup>

CASE VI.—A single woman, aged twenty years, had a scaly eruption occupying the ears, cheeks, nose, and backs of the hands, of seven years' duration, which was regarded as an erythematous lupus. In addition to this eruption the tips of both little fingers were much atrophied, and the patient complained of the fingers "going dead" in cold weather (Cavafy<sup>6</sup>).

CASE VII.—A woman, aged twenty-four years, suffered from daily attacks of asphyxia of the hands, which became black and numb. In addition to these symptoms the patient had acne necrotica of the hands and forearms and an erythematous lupus of the scalp (MacKenzie<sup>7</sup>).

<sup>1</sup> Arch. Surg., i, 22.

<sup>2</sup> British Jour. Derm., vi, 339.

<sup>3</sup> Ibid., xvii, 143.

<sup>7</sup> British Jour. Derm., x, 10.

<sup>2</sup> Ibid., iii, 122.

<sup>4</sup> Ibid., vii, 30.

<sup>6</sup> British Jour. Derm., ix, 328.

CASE VIII.—A woman, aged thirty-four years, who presented unmistakable symptoms of Raynaud's disease, such as alternate pallor and cyanosis of the extremities, had likewise lesions characteristic of erythematous lupus upon the backs of the hands and fingers (Little<sup>8</sup>).

CASE IX.—A woman, aged twenty-six years, had an extensive atrophying erythema of the face, nose, cheeks, and external ears; there were large areas of ivory-white skin dotted over with greatly dilated sebaceous-gland ducts. The scalp was also involved. The hands and feet were always very cold, the fingers much wasted, with impending gangrene of the finger tips. Warde<sup>9</sup> regarded the case as one of atrophic Raynaud's disease associated with erythematous lupus. This same author<sup>10</sup> noted the presence of so-called "dead fingers" in 3 out of a series of 15 cases previously published.

CASE X.—A woman, aged twenty-four years, had suffered from erythematous lupus for twenty years, the disease first appearing on the tip of the nose, spreading thence slowly to the cheeks. Some time later the fingers became affected, and progressive wasting followed. The hands were alternately either "very cold or very hot." The case was exhibited by Sequeira<sup>11</sup> as one of erythematous lupus accompanied by a condition of the fingers "simulating Raynaud's disease."

CASE XI.—A man, aged forty-nine years, had characteristic patches of erythematous lupus on the face, ears, scalp, back of the hands, and fingers. For some time he had complained of his fingers "going dead and white," and actual necrosis of the end of the little finger and lower part of the helix of the right ear had taken place. There were also small eschars on the back of the fingers and on the nose which left slight scars.<sup>12</sup>

CASE XII.—A man, aged sixty-eight years, who had an eruption on the cheeks, ears, and scalp, consisting of red, scaly patches containing atrophic areas, lost several toes by gangrene which had followed an asphyctic condition. The reporters, Engman and Mook,<sup>13</sup> regarded the case as erythematous lupus and Raynaud's disease.

CASE XIII.—A woman, aged thirty years, who in 1894 had been shown at a meeting of the Société Française de Dermatologie et de Syphiligraphie as a case of sclerodermia, six years later developed local asphyxia of the extremities and gangrene with partial destruction of the terminal phalanges, and erythematous lupus. (Hallepeau and Trastour<sup>14</sup>).

In one of the cases reported by Mr. Hutchinson and in my own, suppuration at the roots of the nails occurred at one stage of the

<sup>8</sup> British Jour. Derm., xvii, 104.

<sup>10</sup> Ibid., xiv.

<sup>12</sup> Ibid., xxiii, 182.

<sup>14</sup> Annales de Dermatologie et de Syphiligraphie, 1900, Tome I, 4ième série, p. 634.

<sup>9</sup> Ibid., xv, 279.

<sup>11</sup> Ibid., xix, 427.

<sup>13</sup> Interstate Med. Jour., April, 1909.

disease, a most unusual symptom more likely to have been the result of the vascular disturbances than a part of the erythematous lupus.

In 4 of the cases the symptoms of the lupus followed the vascular disturbances; in the remainder the sequence of the symptoms is not stated. In 1 case (Case V) not less than five years elapsed between the beginning of Raynaud's disease and the appearance of the erythematous lupus.

In some of the discussions which followed the presentation of these cases (nearly all of them were exhibited before English or French dermatological societies) it was objected that the vascular symptoms were not indicative of true Raynaud's disease, chiefly because they were more or less continuous. I do not believe this objection to be well founded, however, since in 6 out of the 14 cases here considered (including my own), nearly 43 per cent., the vascular symptoms were more or less distinctly paroxysmal. Indeed, those cases in which extreme local ischemia was followed by the formation of bullæ and superficial gangrene of the skin of the fingers and toes seem to me to have been typical cases of Raynaud's disease. In the case reported by Engman and Mook, however, it is somewhat doubtful, as the authors themselves admit, whether the gangrene was of the Raynaud type; it seems rather to have been the result of senile changes in the arteries.

The circulatory symptoms very briefly described in the cases which I have here reviewed leave very little room for doubt that in most if not all of them the erythematous lupus was associated with actual Raynaud's disease, or at least, with an affection which simulated that malady so closely as to be practically indistinguishable from it.

The nature of the relationship existing between these two maladies must, for the present at least, remain largely a matter of conjecture; we know too little about their pathogenesis to satisfactorily explain their occasional coexistence. I believe the relationship which undoubtedly exists between them may be best explained by supposing both at times to be due to a common cause, most probably some toxin circulating in the blood, which acts primarily upon the vessel walls producing vasomotor and inflammatory changes in the skin and subcutaneous tissues. Indeed, cases of the kind here considered seem to me to go far in support of the view that erythematous lupus should be regarded as a toxic erythema.

# SOME FEATURES OF THE GROSS ANATOMY OF THE SPINAL CORD AND NERVE ROOTS, AND THEIR BEARING ON THE SYMPTOMATOLOGY AND SURGICAL TREATMENT OF SPINAL DISEASE.<sup>1</sup>

BY CHARLES A. ELSBERG, M.D.,

PROFESSOR OF CLINICAL SURGERY IN THE UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE, NEW YORK.

DURING the last year I have made a number of dissections of the human spinal cord, nerve roots, and membranes in order to study their arrangement and relations. Some of the observations made are recorded in what follows.<sup>2</sup>

*The Structure of the Posterior Roots as the Explanation for the Peculiarity of Root Symptoms at Different Levels.* As is well known, the anterior and posterior nerve roots perforate the dural sheath separately, with a thin septum of dura mater between them. In the cervical region (Fig. 1, A) the nerve bundles of the posterior roots remain distinct until they have passed through the dura. The bundles are spread out like a fan, the broadest part being at the cord. At their origin the bundles are spread out so as to occupy 1 to 2 cm. of the cord; between their origin and the dura they lie closer together, forming a layer 1 to 1½ cm. broad; at the dural openings the nerve bundles are still distinct. In the dorsal and lumbar regions the arrangement is different from that just described; the separate bundles soon combine to form one bundle (Fig. 1, B), which passes outward to the dural opening as the posterior root.

From this arrangement it is clear that in the cervical region a tumor will, for a long time, make pressure only upon a few of the bundles which go to make up a posterior root. In the dorsal and lumbar regions the nerve bundles are united into one nerve near the cord; a tumor in these regions will press upon the whole nerve root from the beginning. Clinical experience agrees with these anatomical facts: the earliest symptoms of pressure upon a cervical nerve root are usually confined to a small area of distribution, one or two fingers for example, while in the dorsal or lumbar region the classical root symptoms extend over entire root areas. It is more exact therefore to distinguish between "root bundle" and "root" symptoms, and this distinction should be of clinical value.

*The Intradural and Extradural Course of the Posterior Roots and its Significance.* A careful dissection of the posterior roots of the

<sup>1</sup> Read at the October (1912) meeting of the New York Neurological Society.

<sup>2</sup> The dissections were done in the anatomical laboratory of the Fordham University Medical School.

spinal cord will show that there are very marked differences in their course at different levels. In the cervical and upper dorsal regions the nerve bundles unite to form the posterior root and pass out of the dural sac at almost a right angle to the cord. They then perforate the dura and enter the posterior ganglion (Fig. 2, *A*). From the ganglion each root passes outward with a slight inclination upward.

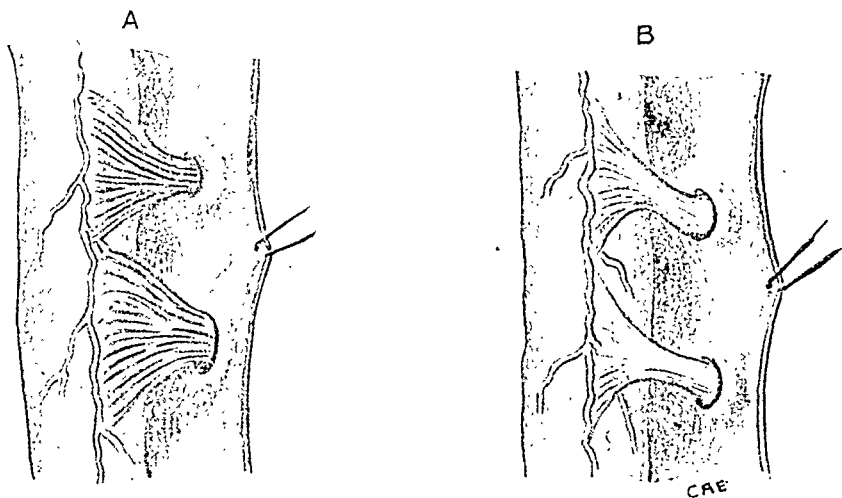


FIG. 1.—*A*, two cervical posterior roots; *B*, two dorsal posterior roots.

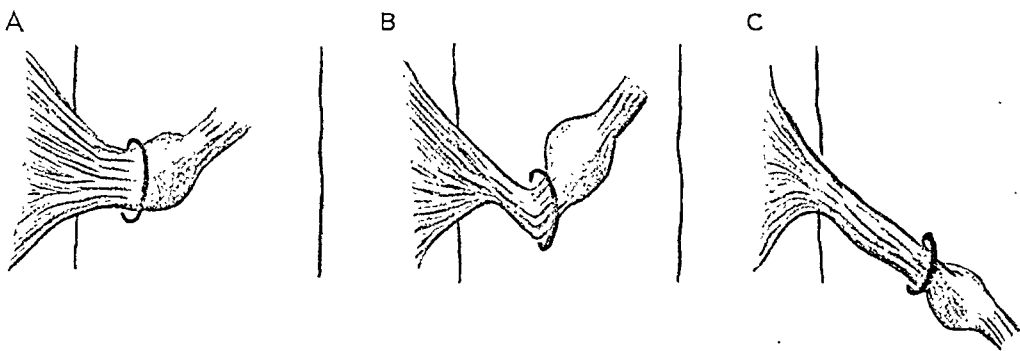


FIG. 2.—The course of the posterior spinal roots. *A*, cervical; *B*, dorsal; *C*, lumbar. Note the marked angle of the dorsal root just before it perforates the dura.

From the eighth cervical to the middorsal region the course of the posterior roots is different. Each root has an inclination downward until it nears the dura; it bends upward at an angle just as it perforates the dura. In the middorsal region this angle is often very acute— $40^{\circ}$  to  $45^{\circ}$  (Fig. 2, *B*). Beyond the ganglion each posterior root passes markedly upward before it divides into its anterior and posterior branches.

In the lower dorsal and lumbar regions the posterior nerve roots pass downward and outward and perforate the dura; beyond



the ganglia the direction remains unchanged until the nerve roots divide into their anterior and posterior branches (Fig. 2, C).

It is easy to understand, when one considers the striking angle in the posterior roots in the dorsal region, that only a slight inflammatory process near the dural opening may be responsible for the occurrence of marked root symptoms.

It is probable that the movements of the vertebral column (bending backward and forward) will increase an existing pressure upon any of the lower dorsal and lumbar posterior roots, because these cannot yield as easily as the upper dorsal roots. Root symptoms in the lower dorsal and upper lumbar regions should become much intensified with forward and backward movements of the vertebral column. To a less degree this must also be the case in the cervical region, although here the bundles of the posterior roots are spread over such a large area that all are seldom pressed upon at the same time. Lateral movements of the spine are apt to increase a root pain on the opposite side and to lessen a root pain on the same side to which the spine is bent. These facts probably have an important bearing upon the occurrence of rigidity of the spine, which is found in patients who have a tumor in the lower dorsal and upper lumbar and also in the cervical cord.

*The Relation of the Ligamentum Denticulatum to the First Lumbar Root and the Surgical Importance of this Relation.* The ligamentum denticulatum is a fibrous band which is derived from and attached to the lateral aspect of the pia mater on the cord midway between the anterior and posterior roots. On each side of the cord the ligament extends from the foramen magnum to the level of the first lumbar vertebra. From its attachment to the cord each ligament extends outward and is attached to the inner surface of the dura by numerous dentations or slips. This ligament divides the subarachnoid space into an anterior and posterior compartment. It is due to this ligament that a tumor which grows on the anterolateral or posterolateral aspect of the cord will press upon only anterior or posterior roots for a long time, and thus give only anterior or posterior root symptoms before the appearance of symptoms of pressure upon the cord itself.

The dentate ligament ends below, at the level of the first lumbar vertebra, in a fork-shaped extremity (Fig. 3, L, D). The outer prong of the fork is usually about 1 cm. long, and is attached by its end to the inner surface of the dura. Sometimes this prong is 3 or 4 cm. long. The inner prong of the fork is attached to the pia on the lateral aspect of the cord and is prolonged downward along the side of the conus to its tip.<sup>3</sup> The first lumbar posterior

<sup>3</sup> The filum terminale is described in the text-books as derived from the pia mater of the cord. It is really the prolongation downward of the inner prong of the fork of the dentate ligament, and is formed by the fusion of the downward prolongations of the ligaments of the two sides.

root rests upon this fork (Fig. 3), so that the "fork" may be used as an anatomical landmark for the identification of the first lumbar root. The posterior roots of the lumbar and sacral nerves are dorsally placed with reference to the fibrous band on the side of the lumbosacral cord and conus derived from the dentate ligament, and can be easily raised up with a probe which is bent to a slight curve. At their origin from the lumbosacral cord the posterior roots lie close together, but when they are raised up with the probe the separate roots can be recognized. If one begins to count from the posterior root which lies on the fork of the dentate ligament, which is the first lumbar, one can easily identify each posterior root.

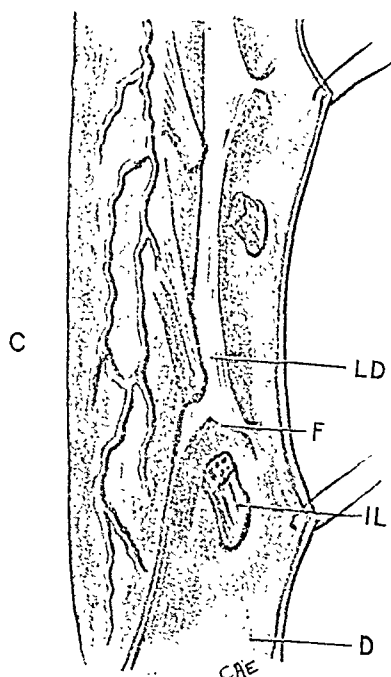


FIG. 3.—The lower end of the ligamentum denticulatum. *LD*, showing the "fork," *F*; *C*, conus; *D*, dura laid open; *IL*, first posterior lumbar root. The root has been divided to show the fork of the dentate ligament.

The importance of these anatomical facts for the operation of division of posterior roots to the lower extremities is clear. In this operation it is usually necessary to divide four or five posterior roots on one or both sides, and, therefore, four or five laminæ have to be removed so that the roots can be identified at the points where they perforate the dural sac. Sometimes it is not easy or certain that one has separated the posterior from the anterior root. To avoid this extensive laminectomy, van Gehuchten, Codivilla, and Wilms and Kolb have suggested that the nerves should be exposed at their origin from the lumbosacral cord by the

removal of three laminæ in the dorsolumbar region. According to these authors, however, it is difficult to recognize the roots to be cut, and there is danger of division of the anterior roots with the posterior ones.

Based upon the anatomical facts above described, I have, in the cadaver, exposed the lumbosacral cord by the removal of the laminæ of the eleventh and twelfth dorsal or eleventh and twelfth dorsal and first lumbar vertebræ, and have been able to recognize and divide the lumbar and sacral posterior roots desired. I desire to recommend the following method for the exposure and division of posterior roots to the lower extremities: Removal of the spinous processes and laminæ of the eleventh and twelfth dorsal vertebræ (and of the first lumbar if necessary) in the usual manner; exposure of the "fork" of the dentate ligament and identification of the first lumbar posterior root; careful elevation of all of the posterior roots of the side to be operated upon (which lie dorsal to the lateral fibrous band on the side of the lumbosacral cord) upon a bent probe passed under them; identification and isolation of the desired posterior roots by counting from the first lumbar root; division of the roots in the usual manner.

---

## BENICE-JONES PROTEINURIA: A REPORT OF FOUR CASES, WITH SOME CHEMICAL AND BIOLOGICAL NOTES.<sup>1</sup>

BY THOMAS R. BOGGS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY; PHYSICIAN-IN-CHIEF, CITY  
HOSPITAL AT BAY VIEW,

AND

C. G. GUTHRIE, M.D.,

INSTRUCTOR IN MEDICINE IN CHARGE OF THE CLINICAL LABORATORY; ASSISTANT RESIDENT  
PHYSICIAN, THE JOHNS HOPKINS HOSPITAL, BALTIMORE

(From the Clinical Laboratory of the Johns Hopkins University and Hospital.)

I. INTRODUCTION. Having had the unusual opportunity of studying, with more or less completeness, 4 cases of Benice-Jones proteinuria, it seems to the writers worth while to record these briefly with some observations on the methods of recognition, chemical properties of the body, and certain biological reactions. The work of Magnus-Levy,<sup>2</sup> Grutterink and de Graaf,<sup>3</sup> Abderhalden and Rostoski,<sup>4</sup> and especially the recent exhaustive con-

<sup>1</sup> Read at the meeting of the Association of American Physicians, May 14, 1912.

<sup>2</sup> Zeit. f. phys. Chem., 1900, xxx, 200.

<sup>3</sup> Ibid., 1902, xxxiv, 393; ibid, 1905, xlvi, 472.

<sup>4</sup> Ibid., 1905, xlvi, 125.

tribution of Hopkins and Savory,<sup>5</sup> have made it certain that this body is not an albumose, but a true protein, yielding the characteristic amino-acids on hydrolysis. The theories as to its origin are quite numerous, but in the light of recent investigations the more important are those which seek its derivation (1) from the proteins of the tissues or blood, (2) specifically from the tissues of the bones, or (3) as a product of abnormal protein metabolism, either endogenous or exogenous. Of these the preponderance of evidence seems to favor the idea that the enormous output of the protein is rather due to the influence of the tumor, or its products, on the tissue metabolism, than the direct product of a relatively small amount of tumor substance present in the body. The great majority of the cases in which this body has been found in the urine have been instances of multiple myeloma, although not all individuals suffering from this disease have exhibited Bence-Jones proteinuria. In isolated instances it has been found associated with other pathological conditions, such as leukemia, chloroma, lymphosarcoma, myxedema, and carcinomatous metastases (1 case). It is also to be noted that some of the reported occurrences associated with leukemia and osteomalacia were subsequently found to be cases of multiple myeloma. The most complete historical review which has come to our notice is that of Rosenbloom.<sup>6</sup>

II. CASE REPORTS. CASE I.—C. F., white, female, aged fifty-four years. Patient of Prof. Gordon Wilson, Baltimore.

Complaint: Rheumatism. Family History: unimportant. Past History: intermittent fever at twenty. When aged twenty-six years fell and hurt left leg, which two years later broke down and ulcerated. Treated several years in the Johns Hopkins Hospital Dispensary. Normally well until October, 1909, when she began to have pains in left leg, which extended to her back and neck, and developed swellings, considered to be rheumatic, in feet and legs, which gradually involved the larger joints of the arms as well. In the winter of 1909 she began to have gastric disturbance, regurgitation of food, not much nausea, no hematemesis, and great wasting. Was considered to have carcinoma of the stomach. Became bedridden, owing to joint troubles and weakness. In May, 1909, she developed severe pains, worse at night, often lancinating in character, in both arms and legs. Gradual atrophy of muscles and stiffness. Severe diarrhea developed in summer of 1910, with abatement of gastric symptoms. Frequent small mucous stools, but no blood. At times incontinence of feces. In the fall and winter of 1910-11, increasing polyuria, with cystitis. Bence-Jones protein was found in the urine by Dr. Wilson in January 1911; it had not been observed in the last previous examination, October, 1910.

<sup>5</sup> Jour. Physiol., 1911, xlii, 189.

<sup>6</sup> (Exhaustive bibliography to 1911) Biochemical Bulletin, 1911, i, 161.

Patient was first seen by us January 20, 1911, at which time she showed great emaciation and rigidity of the extremities. Pupillary reactions normal. There was a moderate stomatitis, with some salivation (not due to mercury). Tongue very thick, pallid, with marked hypertrophy of the papillæ. Buccal mucous membrane opaque and soft. No abnormality in lungs. Heart slightly enlarged, and showed a well-compensated mitral stenosis and insufficiency. Peripheral arteries sclerotic. Pulse of good volume, regular, 80. Blood pressure: systolic, 110 to 120 mm. Hg. Abdomen scaphoid. No abnormal pulsation or peristalsis. No masses made out on palpation. Pelvic organs apparently normal. Extremities: marked thickening about large joints, with limitation of motion and pain on manipulation. No acute inflammatory changes. Terminal phalanges of fingers and toes somewhat enlarged and clubbed. Left tibia was distinctly enlarged throughout the greater part of the shaft, but not rough or irregular. No enlargement of ribs or bone tenderness there or elsewhere in skeleton made out. Rather marked diffuse keratosis in palms and plantar surfaces of feet. Patient was subject to occasional syncopal attacks, in which she apparently had a weak pulse, without convulsions. Marked cutaneous hyperesthesia on palms and soles of feet. At this time there was polydipsia and polyuria. Blood: rather marked secondary anemia. Normal white blood count and differential. Wassermann: negative.

Urine: Amount, twenty-four hours, 2350 c.c.; pale yellow; cloudy; faintly alkaline; specific gravity, 1014; heavy white sediment of granular debris; epithelial cells; no casts, blood, or pus; no sugar; biuret reaction positive; abundant carbonates; uric acid, 0.54 gram; total nitrogen, 12.68 gram; total chlorides, 2.3 gram. (During the last few months of life it was impossible to secure a twenty-four hour specimen, but total amount of urine was about 500 c.c. per day, giving a total chlorides of 3 grams). Polarization after removal of protein negative; diacetic acid and acetone absent; urobilin present; total protein, 2 grams to liter (Tsuchiya); Heller's nitric acid test gave a heavy white ring at contact line; with heat and acetic acid the protein precipitated between 56° C. and 60° C.; partial resolution on boiling and reprecipitation on cooling; filtrate gave no biuret or Adamkiwicz tests; with dilute nitric acid (25 per cent.) characteristic precipitation in the cold, with nearly complete solution on boiling and reprecipitation on cooling.

The case was observed at intervals until her death, May 6, 1912. The polyuria disappeared, partly owing to increasing stomatitis and difficulty in swallowing. Tongue became so large as to practically fill the mouth, deep red in color, marked superficial maceration. In December, 1911, patient was seen again after four months, when a nodule was noted on the anterior border

of the left scapula, hard and apparently continuous with the bone. This gradually increased, reaching the size of a hen's egg before death. In February, 1912, there was tenderness over the third and fourth ribs, left precordium, and axilla, but no nodules were made out. This persisted and increased, ribs becoming eventually definitely nodular, and six days before death they caved in. Coincident with this there developed a pericardial friction rub of great intensity with extreme pain. There was tenderness over most of the thoracic spine, but no nodes were discovered. In April, 1912, nodules were noted over the anterior surface of both elbows about the condyles; there was a brawny induration of the fingers, very like scleroderma, with an extraordinary overgrowth of the horny layers of the skin and a hypertrichosis of the hairs of the face. At this time there was noted a mass extending from the anterior superior spine of the ilium on the left side, half-way to the pubis, which was firm, elastic, and exquisitely sensitive. It caused great pain, referred to the distribution of the anterior crural nerve. A similar, but smaller, mass was felt just behind Poupart's ligament on the right side, near the pubis. These, with the nodules on the other bones, increased with great rapidity during the last four weeks of life, the one on the left ilium reaching the size of a large orange. The inguinal, axillary, and epitrochlear glands became enlarged during this period; they were discrete, firm, and sensitive to the touch. The patient lost all ability to swallow, apparently owing to the enormous swelling of the tongue. Articulation was much impaired. She took no food or water during the last week of life.

X-ray examination, made in February, 1912, with a portable apparatus was unsuccessful, with the exception of the plate of the left tibia, which showed an enlarged, swollen tibia. "There were no absolute areas of bone destruction, but there was a laminated rarefaction, extending throughout the tibia. From the x-ray examination it would be impossible to state definitely that this change was myeloma. In fact, the bone change simulates more closely the changes one sees in Paget's disease."

No autopsy was permitted.

During the entire period of observation (fifteen and one-half months) the urine showed constantly a reaction for Bence-Jones protein.

CASE II.—C. G., white, male, aged fifty-two years. Patient of Prof. H. G. Beck, of Baltimore, who kindly gave us his notes and a specimen of urine after the death of the patient, January 7, 1912.

Abstract of Dr. Beck's notes: "Patient was first seen September 8, 1911. Had been ailing for some months. Complained of shortness of breath, poor memory, weakness, and loss of weight. Physical examination showed arteriosclerosis, hypertrophied heart, aortic

and mitral regurgitation. Blood pressure, 215 mm. Hg. Urine gave a large precipitate with acetic acid and potassium ferrocyanide, but none by heat.

"September 15: Urine contained a large amount of albumose, but no serum albumin.

"October 17: Urine showed precipitate with acetic acid and potassium ferrocyanide, but none on boiling.

"December 2: An attack of acute paroxysmal pulmonary edema. Very cyanotic. Frothy, serous expectoration. These attacks have been noted several times in the last four years, occurring at night and lasting several hours.

"December 10: Urine showed (1) an opacity at 50° C., precipitate at 70° C.; partial clearing on boiling; (2) complete precipitation with two volumes of saturated ammonium sulphate solution; (3) no precipitate in cold with acetic acid.

"December 18: Examination of chest shows small elevations on ribs almost nodular, but no tenderness. X-ray picture of chest does not show any bony changes.

"December 23: Differential leukocyte count normal. Hemoglobin, 58 per cent.

"January 7, 1912: Patient died suddenly after being out all day, apparently of acute dilatation. No autopsy was secured."

Specimen of urine submitted for our examination by Dr. Beck showed characteristic reaction for Bence-Jones protein; precipitation with heat and acetic acid between 54° C. and 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate yielded no test for protein. Typical reactions also were obtained with 25 per cent. nitric acid, and on addition of two volumes of saturated solution of ammonium sulphate. Urine: Clear; acid; specific gravity, 1013; no sugar; total protein, 1½ grams per liter (Tsuchiya); total chlorides, 5 grams per liter; no casts.

CASE III.—S. S., white, male, aged sixty-four years. Patient of Dr. Henry M. Fitzhugh, Westminster, Md. Admitted to the Johns Hopkins Hospital, January 9, 1912, under the care of Prof. T. B. Fletcher.

Complaint: Pain in the left lumbar region and at the navel. Family History: unimportant. Previous History: unimportant. Present Illness: began about two months ago, pain on left side under costal margin, worse in the afternoon and at night. Eructation, no vomiting, no blood in stools.

Examination: Large man, undernourished, slightly anemic. Pupils react normally. Thorax symmetrical. Lungs clear. Heart normal. Pulse normal, no marked peripheral sclerosis. Blood pressure, 180 mm. Hg. Abdomen: no abnormality other than palpable right kidney. Rather marked dermatographia. Exaggeration of deep reflexes. No general glandular enlargement. No enlargement or nodes noted over long bones or ribs. Tenderness

over eleventh and twelfth ribs, on left side. Patient thinks he may have injured this side some six months ago.

Ewald test meal showed marked hyperacidity.

Blood: Red blood cells, 3,800,000; leukocytes, 14,000; hemoglobin, 55 per cent. Differential count shows increase in polymorphonuclear neutrophils.

"X-rays: Lumbar spine negative. Ribs show small vacuolated areas; similar areas in right humerus, due to bone destruction. These areas are sharply defined and there is slight new bone formation around the edge, showing an attempt to limit the disease."

Urine gave characteristic precipitation at 54° C., complete at 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate free from protein. Precipitate insoluble in water, but readily soluble on heating with dilute sodium carbonate solution, latter removed by dialysis, leaving the protein in solution. With 25 per cent. nitric acid there was precipitation in cold with an almost clear solution on boiling, reprecipitation on cooling.

During twenty days of the patient's stay in the hospital the total daily amounts of urine were examined. The Bence-Jones protein was constantly present, and was the only protein demonstrable. The total amount of urine varied between 2000 and 2800 c.c. Specific gravity, 1006 to 1010; total protein, 5 to 7 grams (Tsuchiya); total chlorides varied from 1½ to 4½ grams; coarsely and finely granular casts were found at each examination.

Patient lived about thirteen weeks after leaving the hospital, all the urine being saved and sent to the laboratory, where examination showed the constant presence of the Bence-Jones protein and no other. He grew steadily feebler, with increasing pain, referred to the ribs on the left side. Toward the end there was a development of nodes along the ribs over the precordium, with falling in of the sternum and great pain on breathing and coughing. There was enlargement of the lymphatic glands in the right groin, with great pain in the distribution of the anterior crural nerve. Glossitis was also noted.

No autopsy was permitted.

CASE IV.—E. B., white, female, aged thirty-seven years. Admitted to the Johns Hopkins Hospital April 22, 1912. Died May 9, 1912.

Complaint: rheumatism.

Family History: Father supposed to have died of cancer. Previous History: unimportant.

Present Illness: Began six months before admission with onset of sudden pain in the right hip, which increased so that she was obliged to stop work two weeks later. Walked with great difficulty. After two months a similar trouble appeared in the left hip. Coincident with the joint trouble she noticed increasing nervousness, numbness of hands, and awkwardness. Appetite poor, occasional



vomiting unassociated with pain. Loss of 40 pounds in weight. Four weeks ago she noticed a painful lump in the right breast. Discovery of this lump was not elicited in taking the history, but during the physical examination.

Examination: Patient much emaciated. Slight general pigmentation, most marked in folds of the skin. Mild grade of ichthyosis simplex. Pupils react normally. Lungs clear. Heart normal. Hard, irregular mass in the right breast, with retraction of nipple and some puckering of the skin. Abdomen normal. Reflexes normal. No local or general glandular enlargement. Spine somewhat stiff. Some shortening of the right leg. Tender nodes on the sixth rib of the right side below the breast. Blood pressure, 140 mm. Hg.

Blood: Red blood cells, 4,000,000; leukocytes, 9200; hemoglobin, 74 per cent. Differential, normal. Wassermann, negative.

"X-ray examination shows carcinomatous metastases in head, ribs, both trochanters, both ilia, and right tibia. These metastases are slightly different from what one sees in simple ordinary metastases, in that the areas involved in the bones are sharply limited and do not seem to be invasive in character, as one ordinarily sees. The metastatic areas in the bone, at first glance, present the appearance more of a giant-cell sarcoma, as there is definite new-bone formation around the edge, showing an attempt had been made to limit the disease."

Urine: acid; clear; 1012 to 1018; no sugar; no casts; with heat and acetic acid there is a precipitation at 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate from this reaction gave no tests for protein. Total amounts of urine were studied for nine days, up to forty-eight hours before death. From the combined urines of this period the Bence-Jones protein was isolated by precipitation with two volumes of saturated ammonium sulphate and dialyzation until free from salt, the process being repeated three or four times until a clear, neutral, slightly amber colored fluid was obtained, which gave all the characteristic reactions for Bence-Jones protein in the pure state. This case will be reported in detail elsewhere.

The patient became rapidly weaker and semicomatose, with loss of control of sphincters, difficulty in swallowing, feeble, irregular heart, and death occurred on May 9. No autopsy was secured, but a portion of the femur was removed for section.

"Section of bone and tumor showed epithelial cells of the glandular type in alveoli of different sizes and shapes, surrounded by a rather dense fibrous stroma. In this stroma there are two types of bone areas, old bone showing lacunar absorption by the cancer cells and typical islands of new-bone formation of the endosteal cell type. This was first described by von Recklinghausen as *ostitis carcinomatosa*."

III. GENERAL CONSIDERATION OF THE URINE. As has been so clearly demonstrated by Hopkins and Savory, the specificity of the reaction for Bence-Jones protein is dependent upon the relative stability of its compounds with neutral salts at the boiling temperature, and their instability at lower temperatures (45° C. to 60° C.). The saline concentration has a marked influence on the completeness of the reaction, following closely the laws defined by Hardy for globulins, but differing essentially in the temperature relation. Salts are similarly graded for Bence-Jones protein at 100° C. and for globulins at room temperature. It follows from the above consideration that in applying the heat and acid test to urine for the detection of protein it is important to heat slowly in order that the differences of temperature in the determination of precipitation may be apparent. Should coagulation begin well below the boiling point, more careful examination for the detection of unusual proteins (fibrinogen or Bence-Jones protein) are indicated. If this principle were impressed on students in their training, there is little doubt that many cases would be detected which are otherwise overlooked. In such instances of precipitation well below the boiling point, careful note should be made of any tendency toward clearing on boiling the specimen, and the test repeated with the aid of a water bath and a thermometer. Confirmatory tests are made by treating another specimen with a few drops of 25 per cent. nitric acid—when the initial turbidity in the cold is increased as we approach 60° C., and clears up more or less completely at 100° C., falling out again as the specimen cools. For further confirmation another specimen is treated with two volumes of saturated ammonium sulphate solution when a voluminous precipitation occurs, sometimes quite slowly. These tests are sufficient to establish the presence of Bence-Jones protein. Other tests for Bence-Jones body as it occurs in the urine and when isolated in the pure state may be found on reference to the table in Neuberg, *Der Harn*, 1911, i, 774. If serum albumin is also present it may be determined by first heating the acidified urine to 60° C. for one hour, cooling, filtering until perfectly clear, and boiling the filtrate.

At the outset of this investigation it was our intention to repeat the work of Magnus-Levy, Grutterink and de Graaf, and Abderhalden on the chemical constitution of the body isolated from our abundant material, but this field has been so satisfactorily covered by Hopkins and Savory as to render it unnecessary. A few notes may be made, however, on the relative advantages of the various methods of quantitative separation. For securing material without denaturing the protein, the salting with ammonium sulphate, dialyzing the precipitate, and repeating the process many times, probably yields the best result. This method has the objection that it is time-consuming, and does not free the protein from pigment.

It has been our experience that the urines containing this protein become dark on standing, even when preserved from putrefaction, and great difficulty was experienced in obtaining any precipitate which was not deeply pigmented. Various attempts were made to decolorize the urine before precipitating the protein by use of animal charcoal, Kieselguhr, or carbon black, but we could find no method which yielded a colorless filtrate which did not at the same time remove the greater part or all of the Bence-Jones body. Precipitates treated in thin dialyzing sacs of collodion with running water for weeks held tenaciously to the coloring matter. We also found, as has been noted by other observers, that the protein, when dried *in vacuo*, becomes dark, and these dried precipitates, in our experience, were never completely soluble in distilled water, which we consider an evidence of partial denaturation.

The alcohol precipitation would seem to be limited in its application to the treatment of small volumes, which may be rapidly handled, as the protein soon passes into an insoluble condition on prolonging its contact with the alcohol. Perhaps where facilities for refrigeration on a large scale are available the usefulness of this method may be extended.

For purposes of chemical analysis, where the denaturation, due to heating, is of no moment, we have devised a method which gives excellent results, especially in freeing the substance from pigment and leaving it as a fine dry powder.

The urine is filtered through paper, faintly acidulated with acetic acid, and placed in large bottles in the water-bath, which is kept at 60° C. over night. On removal from the bath, the greater part of the coagulum has settled to the bottom of the containers, which permits of decantation, or syphonage, of most of the supernatant urine. The precipitate is then repeatedly washed in the bottle by shaking with distilled water, and finally collected on a filter, and the washing continued until the filtrate is free from chlorine. The wet precipitate is then spread in Petri dishes in layers not more than 0.5 cm. thick, sealed, and placed in a freezing mixture of ice and ammonium chloride. The frozen material is rapidly transferred to a desiccator, packed in a freezing mixture. The desiccator is then quickly exhausted to a vacuum of 4 mm. or less, when the ice in the precipitate sublimates and is absorbed by the sulphuric acid, leaving the precipitate as a dry, crumbling mass, pale gray to white in color, which is easily pulverized. This material is insoluble in water, but readily dissolves in a dilute solution of sodium carbonate on heating, yielding a water-clear solution, from which the sodium carbonate can be easily removed by dialysis, leaving the protein in solution. Such a solution gives all the characteristic reactions for Bence-Jones protein in the pure state.

In Case I, the longest under observation, after the recognition of the proteinuria the amount excreted varied from 2 to 5 grams

per liter, with an output of 2 or 3 liters in twenty-four hours. In Case III the amount reached as high as 7 grams per liter, with an output of urine about the same as in Case I. The smallest excretion was in Case IV, in which the maximum was 1.5 grams per liter and the average 0.25 to 0.5 gram.

In one of our cases (Case I) we have observed spontaneous precipitation of the protein on standing for several months. These specimens of urine were found on bacteriological tests to be sterile, and the initial alkalinity considerably increased, though the urines were not ammoniacal. This phenomenon has been previously noted by Bradshaw<sup>7</sup> and Rosenbloom,<sup>8</sup> and will be reported fully elsewhere.

Polyuria was present at some time during the course of the malady in all of our cases except one (Case IV).

A striking feature to which attention has not heretofore been called is the great diminution in chloride excretion. The daily output in Case I was 2 or 3 grams; Case II, 5 grams; Case III, 1.5 to 4.5 grams, and in Case IV, 1.2 to 1.4 grams. In one case (Case IV) careful functional tests were made by Drs. Fitz and Rowntree. These showed a phenolsulphonaphthalein excretion of 23 per cent. for two hours; lactose, 8 per cent.; iodide present after seventy-two hours; total chlorides, 0.15 to 0.18 per cent. of the amount ingested. In this case, also, serum albumin was at times present, but no casts were found. In the other cases the Bence-Jones body was the only protein present. In Case III casts were constantly present. None were found in Cases I and II.

IV. BIOLOGICAL REACTIONS. Although the chemical side of the Bence-Jones protein has been fairly completely covered in recent years, the biological investigations have been meager and somewhat conflicting. Borchard and Lippmann<sup>9</sup> have reported the detection of the body in the blood and serum of fasting dogs fed with the substance. In an alkaptonuric patient, Gross and Allard<sup>10</sup> noted a marked increase of homogentisic acid after feeding with this protein, in contrast to results obtained on feeding similar amounts of casein. After injection intravenously and subcutaneously, various authors have reported the presence of specific precipitins in the serum or blood. Rostoski found the reaction did not differentiate the Bence-Jones body from other proteins of human origin. Hopkins and Savory concluded that it is less powerful as a precipitinogen than blood proteins, but that its solutions react slightly with antihuman serum. Massini<sup>11</sup> reported complement fixation with highly potent sera, and was able to differentiate between the blood proteins and the Bence-

<sup>7</sup> Med. Chir. Soc., London, 1898, lxxxi, 259; British Med. Jour., 1898, i, 1136.

<sup>8</sup> Archives of Int. Med., 1912, ix, 255.

<sup>9</sup> Biochem. Zeit., 1910, xxv, 6.

<sup>10</sup> Zeit. f. klin. Med., 1907, xlv, 359.

<sup>11</sup> Deutsch. Archiv f. klin. Med., 1911, civ, 29.

Jones protein. Stokvis<sup>12</sup> noted the appearance of the protein in the urine of dogs after its injection intravenously or by the rectum. In our own experiments we have used the protein obtained by ammonium sulphate precipitation, and have been unable so far to secure a specifically active precipitin, finding only weak reactions of equal intensity for Bence-Jones and human blood serum, but are continuing the experiments with larger doses and with the substance in various states. In all our rabbits, injected intravenously for the production of precipitins, there was commonly anuria for twenty-four hours, followed, in some instances, by the excretion of the protein in the urine in the next forty-eight hours, while after the second injection none of the animals excreted the protein as such.

Intradermal skin tests for sensitization were made, with the same lot of material used for other biological tests, with negative results. The test was applied to a considerable number of individuals, normal persons, and others with various pathological conditions, 4 of whom had bone metastases from carcinoma and sarcoma, inclusive of Case IV. Instillation of the solution into the conjunctiva of Case I did not produce a reaction, nor was any obtained in a case of multiple sarcomatous metastases to the bones. Anaphylactic tests on guinea-pigs are in progress, and other biological investigations with this protein have been undertaken.

V. SUMMARY. From the fact that the writers have observed 4 cases in fifteen months, it would seem that this type of proteinuria is probably more common than the literature would lead one to suppose.

Of these cases, 2 (Case I and Case III) were clinically multiple myeloma, and a third (Case II) was probably of the same type, although we have no objective proof. The remaining case (Case IV) was one of metastatic carcinoma from the breast, and is, we think, unique, as the case reported by Oerum<sup>13</sup> was associated with metastases from a gastric carcinoma. This case will be reported in detail elsewhere. It is especially interesting to note that the detection of the last three followed definitely the interest aroused among local physicians by the presence of the first case, which led them to test the urine of their patients more carefully. We should like to emphasize the fact that the recognition of the Bence-Jones body in the urine in each instance antedated any suspicion of the true nature of the malady, with the exception of Case IV, which was clearly associated with carcinomatous metastases. That this type of proteinuria may be present for some time before any clinical evidence of myelomatosis appears is shown by the first 3 cases noted.

<sup>12</sup> Nederl. Tijds. v. Geneesk., 1891, ii, 136; Maly's Jahr d. Thier. Chem., 1891, xxi, 412.

<sup>13</sup> Ugesk. f. Laeger., 1904, 5 s., xi, 559; Abst. Biochem. Zentrbl., 1904-5, iii, 203.

In Cases I and III the palpable bone tumors developed only late in their course. In Case II death occurred from an intercurrent disease before the appearance of any symptoms suggesting bone involvement, and the skiagrams taken twenty days before death showed normal bone shadows. In Case I the x-ray pictures, as above noted, were imperfect, but showed a laminated rarefaction of the tibia. In Case III the radiologist made a diagnosis of an unfamiliar type of vacuolization in the bones prior to the appearance of any palpable bone tumors, while in Case IV an accurate diagnosis of metastatic carcinoma of the bones was made.

The blood picture in our cases showed nothing abnormal except a secondary anemia. All the patients were aged over fifty years, except the case of carcinomatosis (Case IV). In all there was evidence of great metabolic disturbance in the extreme emaciation. Spontaneous fracture of ribs occurred in 2 cases. The development of metastatic nodes in the soft tissues, as in Cases I and III, is unusual in myelomatosis. Both of these had also glossitis.

In connection with Case I, it is noteworthy that there was marked hypertrichosis, macroglossia, keratosis of the palms, and soles, and scleroderma. These point to some disturbance of the internal secretions which may have been coincidental. Fitz<sup>14</sup> has reported, however, Bence-Jones proteinuria in myxedema.

In regard to possible changes in the kidney, we can say nothing from the morphological standpoint, as we had no autopsies, but would merely call attention to the striking fact that the kidney was permeable for the Bence-Jones protein, but held back serum albumin (except just before death in Case IV), and in all cases there was a striking diminution in the chloride excretion. These would seem to indicate functional disturbance of the kidney rather than a true nephritis.

In closing we take opportunity to express our thanks to Drs. Wilson, Beck, Fitzhugh, and Fletcher for access to their cases, and to Profs. Barker and Halsted for use of material in their services. Special thanks are due Dr. Baetjer for his interest in the radiographic studies, and to Drs. Fitz and Rowntree for the functional tests.

<sup>14</sup> AMER. JOUR. MED. SCI., 1898, cxvi, 30.

# FURTHER EXPERIENCES WITH THE COMPLEMENT FIXATION TEST IN THE DIAGNOSIS OF GONOCOCCUS INFECTIONS OF THE GENITO-URINARY TRACT IN THE MALE AND FEMALE.<sup>1</sup>

BY HANS J. SCHWARTZ, M.D.,

INSTRUCTOR IN CLINICAL PATHOLOGY AND CLINICAL INSTRUCTOR IN DERMATOLOGY IN CORNELL UNIVERSITY MEDICAL SCHOOL, NEW YORK,

AND

ARCHIBALD MCNEIL, M.D.,

DEPARTMENT OF HEALTH RESEARCH LABORATORIES, NEW YORK.

(From the Department of Clinical Pathology of the Cornell University Medical School, New York.)

IN a previous paper<sup>2</sup> attention was drawn to the value of the serum diagnosis of gonococcus infections in general. We there showed that in chronic gonococcus infection, even though limited to the genito-urinary tract, an antibody specific for the gonococcus could readily be detected in the blood. Our experimental work showed that the secret of success lay in the use of a polyvalent antigen, on account of the fact that the different strains of the gonococcus seemed to differ considerably one from the other.

We then gave the results of the application of the test to a total of 324 human sera. These results showed that the complement fixation test (using a polyvalent antigen) for gonococcus antibodies should prove an addition to our methods of diagnosing between the various chronic conditions arising from gonococcus infection and similar conditions due to other causes. In addition we pointed out that the complement fixation test might be a distinct aid in finally deciding as to whether a patient was cured of his or her gonococcus infection, inasmuch as the blood test was positive in a certain percentage of cases where other means of diagnosis failed.

Finally, we stated that, in our opinion, the facts at hand seemed to prove conclusively that a positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

Since then articles by Swinburne,<sup>3</sup> Keyes,<sup>4</sup> Schmidt,<sup>5</sup> and Gradwohl<sup>6</sup> have appeared corroborating our results in all essential particulars.

**TECHNIQUE.** The antigen used at the present time is prepared as follows: The various strains of gonococci are grown on salt-free

<sup>1</sup> Read by invitation before the American Association of Genito-urinary Surgeons, Philadelphia, June 7 and 8, 1912.

<sup>2</sup> AMER. JOUR. MED. SCI., May, 1911.

<sup>3</sup> Arch. of Diag., July, 1911.

<sup>4</sup> AMER. JOUR. MED. SCI., Jan., 1912.

<sup>5</sup> Trans. Amer. Urol. Assoc., 1911.

<sup>6</sup> Amer. Jour. Derm. and Syph., Urinary Diseases, June, 1912.

veal agar, neutral in reaction to phenolphthalein; twenty-four-hour old cultures are washed off the agar slants with distilled water and the resulting suspension is heated for two hours in the water-bath at 56° C. It is then centrifugated and passed through a Berkefeld filter. No salt is added to this antigen until it is desired to use it, when it is made up to 0.9 per cent. strength by adding one part of 9 per cent. saline solution to nine parts of antigen.

The antigen is best preserved in small quantities in sealed tubes, heated to 56° C. for half an hour on three successive days, to insure sterility. If possible, the antigen is standardized with a known positive serum from a clinical case. If this is impossible, immune rabbit serum may be used, provided that the minimum amount of the serum which will completely fix complement is used. An antigen titrated with a highly immune rabbit serum may show perfect fixation in an amount that would fail to show any fixation with the average clinical case, on account of the lower antibody content of the latter. Antigens prepared as above will keep almost indefinitely if kept in sealed tubes free from contamination. We now use only the antisheep hemolytic system, but in other respects the technique is the same as described in our previous paper, except that we now use all the ingredients in one-tenth the quantity used in the original Wassermann technique for syphilis.

We may say that for the last few months we have used the gonococcus antigen prepared by Parke, Davis & Co., along with our own, and so far it has given satisfactory results.

**SIGNIFICANCE OF A POSITIVE AND A NEGATIVE REACTION.** As already stated, we found a positive reaction to be specific for the gonococcus with the sole exception of meningococcus infection.

Our positive results in meningococcus infection were obtained when using a highly immune anti-meningococcus serum prepared according to Flexner's method. We have since tested the serum of several patients suffering from cerebrospinal meningitis, with uniformly negative results. It would, therefore seem that, clinically, the complement fixation test for gonococcus infection is absolutely specific for the gonococcus. As is well known, the Wassermann reaction is not absolutely specific for syphilis. A positive reaction is obtained in various other diseases, notably leprosy, chronic malaria, frambesia, etc., probably due to the fact that the serum in these diseases contains abundant lipotropic substances. In the gonococcus complement fixation test we have a true antigen-antibody combination, inasmuch as the antigen is prepared from the specific infecting organism of the disease in question. In the Wassermann reaction we do not have this true antigen-antibody combination. The so-called antigens in the Wassermann reaction are present in the lipoidal substances of the tissues whether derived from luetic or non-luetic human subjects or animals. This probably accounts for the superior specificity of the gonococcus complement fixation test.



A negative reaction does not, of course, exclude the possibility of gonococcus infection being present, in the same way as a negative Wassermann reaction does not exclude the possibility of syphilitic infection. In this connection, however, there are two facts to be taken into consideration:

1. In the late lesions of syphilis, in common with the other infectious granulomas, there is a distinct tendency to the formation of a more or less well-marked connective-tissue capsule surrounding the lesion. As a result, there is arrested activity on the part of the spirochetæ, a less amount of toxin is elaborated, the connective-tissue capsule offers some resistance to the free absorption of toxins, and, as a result, there may be lessened antibody formation. This condition does not obtain in gonococcus infection, as the lesions here do not tend to become encapsulated.

2. The Wassermann reaction is definitely obscured by recent mercurial treatment. There is no treatment which thus obscures the complement fixation test for gonococcus infections. On account of these two facts we think that more importance may perhaps be attached to a negative reaction in testing for gonococcus infection than is to be attached to a negative Wassermann test for syphilis.

**TIME OF APPEARANCE OF A POSITIVE REACTION.** A positive reaction is not to be expected earlier than about the fourth week of the disease, and then only in acute cases with some complication such as acute prostatitis, gonococcus arthritis, etc. For example, in one case of acute gonococcus arthritis coming on three or four days after the onset of the urethritis the blood was negative (though very slowly) on the twenty-first day, and strongly positive on the twenty-eighth day from the first appearance of the urethral discharge. In another similar case the blood was negative on the seventeenth day and strongly positive on the twenty-fifth day of the disease.

**TIME OF DISAPPEARANCE OF A POSITIVE REACTION AFTER CURE.** It is, of course, evident that the antibodies must persist in the blood for some time after the patient is actually cured. How long they persist is a difficult question to answer precisely. That they do not persist indefinitely we are quite certain. Torrey<sup>7</sup> has shown that the complement fixatives in the blood of a rabbit immunized to the gonococcus begin to be eliminated ten days after the date of the last inoculation and continue to be eliminated rapidly from the tenth to the fiftieth day, after which they are only found in small quantities.

Our own experiments with rabbits confirm these results. After the fiftieth day from the date of the last inoculation only a reaction can be obtained. This is a reaction to which we attach no importance.

<sup>7</sup> Jour. Med. Research, 1910, No. 1, p. 95.

Clinically, we have seen one case in which a two-plus reaction changed to a negative in five weeks after cure. The majority of cases, however, take somewhat longer. As a rule, we think a negative reaction should be obtained seven or eight weeks after cure. In other words, if a positive reaction is obtained seven or eight weeks after clinical cure we think that the patient should be looked upon as still harboring gonococci.

RELATIVE VALUE OF THE COMPLEMENT FIXATION AND BACTERIOLOGICAL METHODS OF DIAGNOSIS IN CHRONIC AND DOUBTFUL CASES, AND THE TECHNICAL DIFFICULTIES CONNECTED WITH THE TWO METHODS. As we have already stated, the complement fixation test is specific for the gonococcus. A positive reaction must therefore be looked upon as absolute proof of a focus of gonococcus infection somewhere in the body. What constitutes absolute proof of the gonococcus bacteriologically? Certainly not a smear stained with methylene blue. A Gram stain, properly made, can be accepted where the gonococci are abundant; but in chronic cases, with few organisms present, it cannot be accepted as absolute proof. Among the sources of error may be mentioned the *Micrococcus catarrhalis*; degeneration forms of Gram-positive cocci which not infrequently do not retain the Gram stain, and according to Adami<sup>8</sup> the *Trichomonas vaginalis* and some aberrant forms of the *Bacillus coli*. All authorities are agreed that in doubtful cases culture methods constitute the only absolute proof.

There is little doubt that the technique of isolating the gonococcus in culture is far more difficult than the technique of a complement fixation test. In the first place, the bacteriologist may err, as Dr. E. L. Keyes, Jr.,<sup>9</sup> well says, "through his own fault or through the fault of the clinician who submits the specimen to him, and the precision of his diagnosis depends upon a well-prepared specimen as much as upon his own skill." The prostate and vesicles must be thoroughly massaged and the specimen must be fresh, as it is probable that the gonococcus cannot be cultivated if allowed to stand in cool urine for half an hour. In addition, the gonococcus grows only on special media, and culture may fail on account of the presence of other rapidly growing organisms which either inhibit the growth of the gonococcus or render its isolation impossible. This is especially the case in women.

In connection with the complement fixation test, the only real difficulty lies in obtaining and carrying the various strains of the gonococcus necessary for the preparation of a good antigen. Apart from this, if the serologist carefully and frequently titrates the various reagents used in the test, a matter neither difficult nor time-consuming, the technique of the complement fixation test is comparatively simple.

All the above facts must be taken into consideration in judging

<sup>8</sup> Principles of Pathology, ii, 782.

<sup>9</sup> Loc. cit.

as to the relative value of the bacteriological and complement fixation methods of diagnosis. In the presence of a positive complement fixation test and negative bacteriological findings, we think the fixation test should be accorded its full value. In the presence of a negative complement fixation test and positive bacteriological findings, we think the bacteriological findings should be accepted as correct only if the proof is absolute—namely, isolation of the gonococcus in culture.

In connection with the above statements the limitations of the complement fixation test, to be detailed later, are, of course, to be borne in mind. In all cases we think that in the interests of the patient both methods of diagnosis should be used.

# I. GONORRHEAL URETHRITIS, GONOCOCCI PRESENT.

No. of cases.	Duration.	Reaction.
3	2 weeks . . . . .	—
4	3 weeks, both urines cloudy . . . . .	+
1	4 weeks, both urines cloudy . . . . .	+
1	4 weeks, marked prostatic involvement . . . . .	+++
2	4 weeks, gonococcus arthritis, 3 weeks . . . . .	+++
1	5 weeks, both urines cloudy . . . . .	+
2	6 weeks, both urines cloudy . . . . .	+
1	7 weeks, prostatic abscess . . . . .	++
2	8 weeks, both urines cloudy . . . . .	++
1	8 weeks, prostatic involvement . . . . .	++
1	8 weeks, second urine clean . . . . .	—
1	10 weeks, second urine clean . . . . .	—
4	12 weeks, prostatic involvement . . . . .	+++

*Remarks.* The above illustrates the gradual development of a positive reaction.

In anterior urethritis, whether acute or chronic, a positive reaction is not obtained. Cases of urethritis remaining confined to the anterior urethra are, of course, rare. Most authorities agree that in the great majority of cases the posterior urethra is involved. One of Dr. Keyes' cases, however, had had urethritis for ten weeks. The first urine passed was slightly cloudy, the second urine, passed after the prostatic massage was quite clear and microscopic examination revealed no gonococci. There was a thin mucoid discharge at the meatus, in which gonococci were found, and they were also obtained in culture. Culture made from the urine passed after the prostatic massage was sterile. Here the infection was probably confined to a few glands in the fossa navicularis and there was not enough absorption of toxins to stimulate antibody formation. This case is cited here in order to bring out the point that probably a positive reaction is never found when the disease remains confined to the anterior urethra.

A weakly positive (one-plus) reaction first makes its appearance in the third week of the disease and only then when the posterior urethra is affected. In the ordinary case of acute antero-

posterior urethritis without complications running on to cure in six to eight weeks, the most that can be expected is a one-plus reaction. In the absence of complications a strong positive (two-plus) reaction does not make its appearance until the disease has lasted about eight weeks. A two-plus or three-plus reaction can be obtained as early as the fourth week, when there is some definite complication such as acute prostatitis, arthritis, etc. In fact, a three-plus reaction probably is not found when the disease is limited to the genito-urinary tract unless there is some definite implication of the deeper structure.

The fact that a positive reaction is not obtained in the early weeks of the infection, should prove an aid in differentiating between a fresh infection and the recurrence of an old, apparently cured, one. This also suggests possible medico-legal application of the test. Case XXI of Dr. Keyes'<sup>10</sup> series, illustrates this point. This was a married man who had infected his wife with gonorrhea some months previously. Both were treated and finally declared cured, and the blood test made some months later was negative in both. Two weeks later he returned, absolutely denying extramarital exposure, but with a fresh gonorrhea two weeks old. Both he and his wife had the blood test made again, and both were negative. Four weeks later he was positive and she was negative, and she remained clinically cured. As Dr. Keyes says: "The development of a positive reaction in him showed the infection to be a fresh one due to extramarital exposure, in spite of his fervent denials." Dr. Keyes informs us that some six months later the husband finally confessed to the truth of the preceding statement.

Undoubtedly, however, the cases of greatest importance to the clinician, especially when the question of marriage arises, are those of chronic urethritis, prostatitis, and seminal vesiculitis following gonorrhea. Prostatitis is probably the most frequent and important complication. In many such cases we have obtained a positive complement fixation test when bacteriological methods have left us in doubt as to the presence or absence of the gonococcus. It is in such cases that we think the complement fixation test will prove an addition to bacteriological examination.

## II. CHRONIC ANTEROPOSTERIOR URETHRITIS.

1. Gonococci present: In our experience in these cases a positive reaction is practically constantly found and we do not propose to enter into any detail here. We can only recall one case out of a great many examined in which the complement fixation test failed. This was a case of urethritis, followed in a few days by a multiple gonococcus arthritis. The blood was negative on the thirteenth, twenty-sixth, and thirty-sixth days of the disease,

<sup>10</sup> Loc. cit.

and positive on the sixty-first day. By that time, however, the patient had received eight injections of gonococcus vaccine which would have rendered the reaction positive in any case.

2. Gonococci doubtful: This group includes 5 cases in which both smear and cultural examinations were made, but in which the findings were inconclusive.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows fairly abundant sediment of pus. Smears show a few Gram-negative extracellular cocci. Plates show staphylococci and pseudodiphtheria bacilli and a few Gram-negative cocci (gonococci?). Complement fixation test positive.

Case II. Gonorrhea fourteen months ago. Urine after prostatic massage shows scanty mucous sediment with a moderate number of pus cells. Smears show Gram-negative and Gram-positive bacilli, Gram-positive cocci and very few Gram-negative cocci. Plates show Gram-negative bacilli, staphylococci, and streptococci. Complement fixation test positive.

Case III. Gonorrhea five years ago. Urine after prostatic massage shows moderate number of pus cells and a few Gram-negative extracellular cocci. Plates contaminated. Complement fixation test positive.

Case IV. Gonorrhea three years ago. Urine after prostatic massage, shows slight mucous sediment, few pus cells, and a few atypical extra-cellular Gram-negative cocci. Plates sterile. Complement fixation test negative.

Case V. Gonorrhea three years ago. Urine after prostatic massage shows moderate number of pus cells. Smears show many Gram-positive cocci and a few Gram-negative extra- and intra-cellular diplococci. No Gram-negative cocci. Complement fixation test positive.

3. Gonococci negative, both in smear and culture. Nine cases giving a history of gonococcus infection from nine months to fifteen years previously were negative by the complement fixation test thus agreeing with the bacteriological examination. Two cases gave a positive complement fixation test.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows a moderate number of pus cells. Smear shows Gram-positive cocci. No Gram-negative cocci. Plates show staphylococci and streptococci. No Gram-negative cocci.

Case II. Gonorrhea three months ago. Urine after prostatic massage shows few pus cells. Smears show Gram-positive cocci and Gram-negative bacilli. Plates show streptococci and Gram-negative bacilli. In this case the positive complement fixation test was very possibly a fading reaction.

4. Gonococci negative in smear only, cultural examination not made. Six cases, giving a history of gonococcus infection from seven months to five years previously were also negative by the complement fixation test. One case, giving a history of gonococcus

infection two years previously, was positive by the complement fixation test.

5. Cases in which gonococci were not searched for. These cases all had symptoms of chronic urethritis believed to be postgonorrheal. The duration of the urethritis varied from two to fifteen years. Thirty-one cases were examined, of which 10 or 32.2 per cent. gave a positive reaction.

The cases included in groups 2, 3, 4, and 5, were all regarded clinically as postgonorrheal. If now we group all these cases together, we find that out of 54 cases examined a positive result was obtained in 17 or 31.4 per cent. These figures closely correspond with those reported by Keyes<sup>11</sup> in postgonorrheal urethritis, in 26 cases carefully examined by smear and culture gonococci were found in 8 or 30.7 per cent. In a number of our cases, however, the result of smear and cultural examinations was suspicious, but inconclusive, as cited in group 2, whereas the complement fixation test was definitely positive or negative. Herein, in our opinion, lies one great advantage of the complement fixation test.

### III. VERUMONTANUM DISEASE. GONOCOCCI NOT FOUND.

Twenty-two cases of disease of the verumontanum have been examined. Of these, 21 admitted gonorrhea from one to ten years previously. Four of the 21 gave a positive reaction and 17 a negative reaction. One case, cited in our previous paper, absolutely denied gonorrhea, but had given a positive result on two separate occasions. After six months' treatment he was found to be negative.

### IV. CHRONIC PROSTATITIS

1. Gonococci present: Three cases were examined, all of which gave a positive complement fixation test.

2. Cases giving a definite history of gonorrhea—gonococci not searched for.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
5 weeks to 1 year ago . . . . .	31	20	11
2 years ago . . . . .	19	9	10
3 years ago . . . . .	12	5	7
4 years ago . . . . .	5	2	3
5 years ago . . . . .	7	0	7
6 years ago . . . . .	3	2	1
7 years ago . . . . .	5	2	3
8 years ago . . . . .	2	1	1
10 years ago . . . . .	3	1	2
12 years ago . . . . .	6	3	3
14 years ago . . . . .	1	0	1
20 years ago . . . . .	3	1	2
30 years ago . . . . .	1	0	1
3. Gonorrheal history doubtful . . . . .	9	2	7
4. Gonorrhea denied . . . . .	2	0	2

<sup>11</sup> Loc. cit.

In group 2 we have a total of 98 cases of chronic prostatitis in which a definite gonorrheal history was obtained. Of these, 46, or 46.9 per cent., gave a positive reaction.

It will be noted that we have obtained positive results in cases where the last gonorrheal infection was stated to be anywhere from six to twenty years ago. We, of course, do not vouch for the accuracy of the patients' statements in that regard. Opinions vary greatly as to the length of time the gonococcus may persist in the genito-urinary organs of the male and female. We feel that a patient giving a positive complement fixation test should be looked upon as still harboring gonococci irrespective of the date of the last gonorrheal infection.

V. SEMINAL VESICULITIS.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
6 months ago . . . . .	1	0	1
2 years ago . . . . .	3	1	2

VI. CLINICALLY CURED CASES.

In this group we have included only such cases as have been looked upon as clinically cured for at least three months. This was done so as to avoid the possibility of including cases which actually were cured but might still present a fading reaction.

We have examined in all 165 cases, of which 22, or 13.2 per cent., gave a positive reaction. These figures correspond closely with those reported by Schmidt<sup>12</sup> at a recent meeting of the American Urological Society. Out of 42 cases examined he obtained a positive result in 5, or 11.9 per cent. Keyes<sup>13</sup> estimates about 4 per cent. of clinical error in cases apparently cured, basing this statement on the results of laboratory investigation of 86 patients clinically cured of urethral gonorrhea. Thirty-six of his cases were examined by the complement fixation test, and 77 by smear and culture.

In our previous paper we reported 43 per cent. of positive results in cases of this group. Our first series contained all cases examined from the very beginning of the investigation, before we had any definite idea of the possibilities of the test and cases were classed as clinically cured which more rigid examination would probably have excluded from that group. The cases here reported have all been very thoroughly examined before being classed as clinically cured and we think that 13.2 per cent. represents fairly accurately the clinical error in such cases. The importance of these results when the question of marriage arises needs no emphasis here.

<sup>12</sup> Jour. Amer. Med. Assoc., April 27, 1912, p. 1307. <sup>13</sup> Loc. cit.

## VII. WOMEN.

The diagnosis of gonococcus infection in women is well known to be very difficult and uncertain, and bacteriological methods of diagnosis are not of any great assistance, except in the acute forms which are relatively rare. In subacute and chronic forms, gonococci are generally very scanty. They are to be found more particularly in the discharge from the urethra and cervix. However, the great number and variety of other organisms present in such discharges renders the absolute demonstration of the gonococcus exceedingly difficult both in smear and culture. Very often both clinical and bacteriological examinations leave one in doubt and the diagnosis of chronic gonococcus infection must be only a probable one. Hence, we feel that in women the complement fixation test should prove a distinct addition to our means of diagnosing chronic gonococcus infection.

EXTENT OF INVOLVEMENT NECESSARY TO OBTAIN A POSITIVE REACTION. It will be remembered that in discussing the question of gonococcus infection in the male, it was stated that a positive reaction was not to be obtained if the disease remained confined to the anterior urethra. There had to be at least some involvement of the posterior urethra in order to obtain a positive reaction. In gonococcus infection in the female, the organs chiefly involved are the urethra and Skene's glands, Bartholin's glands, the cervix, the uterine tubes, ovaries, and peritoneum. The vagina very commonly escapes, especially in the adult. In children the vaginal mucosa is much more likely to be infected, as in the young, the pavement epithelium is softer and more like columnar epithelium. Hence, the frequency of gonococcus vulvovaginitis in children.

We have obtained positive reactions in cases of peritonitis, in tuboövarian disease, and in disease of the cervix.

We have also obtained a positive reaction in 2 cases of vulvovaginal abscess, but in the absence of abscess formation, we doubt if a positive reaction will be obtained unless there is some infection of the cervix. In other words, we think a negative reaction will probably be obtained if the disease is limited to the urethra, Skene's glands, and Bartholin's glands. Such cases are doubtless rare, as in the great majority of cases of chronic gonorrhea in the female the cervix is involved. Still we feel that the possibility deserves mention here. In gonococcus infection in young children, the vulva, urethra, and vagina are chiefly affected; only rarely are the cervix, corpus uteri, and tubes involved. We have examined 10 cases of vulvovaginitis in children aged under five years. In all the gonococcus was demonstrated in smear and culture. In all the complement fixation test was negative. This tends to support our opinion that a positive complement fixation will not be obtained unless there is involvement of the cervix.



The important role which the gonococcus plays in the production of pelvic disease in women, scarcely needs mention. Destructive inflammation of the tubes and ovaries, with peritonitis, is common, as is also gonococcus infection of the bladder with secondary ascending infection of the ureters and kidneys.

Finally, on every general maternity service cases of gonorrheal ophthalmia occur from time to time. Statistics show that even with the use of silver nitrate in the eyes, this disease occurs as often as once in every 200 cases. Apart from the possible serious effects upon the eyes of the child itself, there is always great danger of the infection spreading to other infants and nurses. Therefore, on account of the unreliability of the smear and cultural methods of diagnosis of subacute and chronic gonococcus infections in women, we think that the complement fixation test should find a distinct place in gynecological conditions, and that on general maternity services it will be of use in the prevention of gonorrheal ophthalmia.

We have not applied the test as extensively in diseases of the genito-urinary tract in the female as we have in the male. This was principally on account of the fact that our chief object was to study the possibilities and limitations of the test. This could be done much more satisfactorily in the male because the course and development of gonococcus infection is much more readily studied in the male. Furthermore, the complement fixation test could be more thoroughly controlled by bacteriological examination in the male than in the female.

The statistics which follow give, however, a fair idea of the field of usefulness of the complement fixation test in gynecological conditions.

Clinical diagnosis.	Positive.	Negative.
Urethritis and endocervicitis;		
(a) Gonococci present . . . . .	9	0
(b) Gonococci not found . . . . .	8	3
Gonorrhea clinically cured . . . . .	1	4
Chronic gonorrhea, gonococci not found . . . . .	2	0
Gonorrheal vulvovaginitis; girls under five years, gonococci present . . . . .	0	10
Salpingo-oöphoritis . . . . .	9	3
Pyelitis clinically considered gonorrheal . . . . .	2	0
Vulvovaginal abscess; gonorrheal . . . . .	2	0
Pelvic peritonitis . . . . .	3	1
Pregnancy; gonococci present . . . . .	1	0
Pregnancy; gonococci not found . . . . .	14	40
Miscellaneous cases from the clinic; lacerations, displacements, etc. . . . .	13	50
Pyosalpinx . . . . .	3	4
Pelvic abscess . . . . .	0	2

One case clinically diagnosticated as pyösalpinx, and giving a negative complement fixation test, was found at operation to be a case of cystic ovary with normal tubes.

One case diagnosticated as pelvic abscess, and giving a negative

complement fixation test, was found at operation to be a tubo-ovarian abscess from which the colon bacillus was obtained in pure culture.

1. CONCLUSIONS. A positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

2. A negative reaction does not exclude gonococcus infection but, for the reasons stated, should be accorded considerable importance.

3. A strong positive reaction is not to be expected earlier than about the fourth week, and then only in very acute cases with some complication.

4. A positive reaction is not obtained if the disease is limited to the anterior urethra.

5. A positive reaction does not entirely disappear until seven or eight weeks after cure.

6. In other words, if a strong positive reaction is obtained seven or eight weeks after apparent clinical cure, the patient should be looked upon as still harboring gonococci.

7. In chronic cases, isolation of the gonococcus in culture is the only absolute, bacteriological proof of gonococcus infection.

8. The technique of a complement fixation test is simpler than that of isolation of the gonococcus in culture and the possibilities of error are less.

9. In cases regarded clinically as postgonorrheal, a positive reaction is obtained in 31.4 per cent.

10. In 62 cases of chronic prostatitis giving a history of gonococcus infection within three years, a positive reaction was obtained in 54.8 per cent.

11. In 165 cases looked upon as clinically cured for at least three months, a positive reaction was obtained in 13.2 per cent.

12. In women, a positive reaction is probably not obtained unless there is at least some involvement of the cervix.

13. On account of the unreliability of the bacteriological diagnosis of gonococcus infection in women, the complement fixation test should prove of special usefulness in gynecological conditions.

NOTE.—Since this paper was written, other articles on the subject have appeared, as follows: Smith, *Lancet-Clinic*, Aug. 3, 1912; O'Neil, *Boston Med. and Surg. Jour.*, Oct. 3, 1912; Gardner and Clowes, *New York Med. Jour.*, Oct. 12, 1912. These articles also corroborate the results of previous workers.

## INDICANURIA.

BY WILLIAM GERRY MORGAN, M.D.,

PROFESSOR OF GASTRO-ENTEROLOGY, GEORGETOWN UNIVERSITY, WASHINGTON, D.C.

THE presence of excessive amounts of indican in the urine is so frequent that we have all seen hundreds of such cases. I have taken occasion to go over my records of all patients seen in 1911 whose urine showed an excess of indican, and will present the observations which I have made from the study.

Indican, or the indoxyl sulphate of potassium, as is well known, is non-toxic. The indol from which it is formed is but slightly toxic, Herter claiming that small doses may produce in man frontal headache, mental irritability, insomnia, etc. Wooley and Newburg, in a preliminary report of their experiments on the result of the injection of animals with indol, found that examination of the adrenals showed the medulla hyperplastic and apparently hypertrophic, and that the evidences of chromaffin activity increased in proportion to the number of injections. They also found slight interstitial changes in the kidneys.

It may be, therefore, that, *per se*, excessive indol absorption from the intestine over a considerable length of time may, by stimulating the adrenals to increased secretion, be instrumental in producing arteriosclerosis and chronic nephritis. Be that as it may, we make use of the indican test because we believe that in most cases the various products of bacterial decomposition, or bacterial digestion as expressed by Combe, of proteids in the intestines, that is, the aromatic bodies (including indol, skatol, phenol, and the cresols), and toxalbumins develop and are absorbed with a certain relationship. Since we have no means at present of determining the quantity of the more definitely poisonous toxalbumins, we are forced to estimate their amount by the degree of putrefaction, as evidenced by the amount of indican excreted in the urine.

In my laboratory the ordinary test for indican employed is: 10 c.c. HCl, 10 c.c. of 1 per cent. solution of potassium chlorate, 3 drops of which is added to the urine and shaken up with 5 c.c. of chloroform. The blue color in the chloroform indicating an excess of indican is arbitrarily graded as to intensity from plus one or sky blue to plus six, the highest grade which we encounter, a very black blue.

Indol results from bacterial digestion or putrefaction of proteids, the bacteria taking up the work of splitting the proteid molecule where the enzymes have left off. It is fairly certain that the lower ileum is the chief laboratory for the formation of this end-product, and that the principal absorptive seat is the colon. Considerable

putrefaction can undoubtedly occur without the occurrence of indicanuria, due probably to non-absorption from the colonic mucous membrane or to some protective mechanism in various organs of the body, as the liver. On the other hand, loss of continuity of the surface of the colon may result in considerable quantities of indican being present in the urine where the degree of putrefaction could hardly be considered enough to account for it. While not all cases of intestinal putrefaction result in indicanuria the writer believes that excessive indican in the urine always indicates abnormal functioning, and that the cause should, if possible, be found and eliminated.

During the year 1911, 148 patients showed indican transitory or more persistently. The cases were about equally divided between the sexes, 73 occurring in females and 75 in males. Usually the indican was incidentally present during treatment for other gastro-intestinal conditions. In some it was accidental or transitory, in some recurrent, in others more or less constant, a definite part of the clinical picture, but still associated with other pathological processes, and in several it was present without evident cause. The latter are the cases of true indicanuria, idiopathic or perhaps to be classed as pure intestinal auto-intoxication. I agree with Baar, who considers these cases of true intestinal auto-intoxication as rare. He specifies that examination of the whole body, the stomach contents, the feces, and blood must yield no abnormal findings.

Of the new patients consulting me in 1911, 89 showed indican in the urine on the regular routine examination at the time of consultation. Of this number 24 showed plus 1, 30 plus 2, 22 plus 3, 9 plus 4, 3 plus 5, 1 plus 6.

In a former paper the writer stated that indicanuria is several times more prevalent in Washington from January 1 to July 1 than during the remaining months of the year, the explanation for which will be mentioned later. Of the 148 cases, 92 occurred in the first six months of the year. A consideration of the distribution of the 89 new patients does not indicate this state of affairs so plainly. They consulted me as follows: In January, 10; February, 10; March, 6; April, 10; May, 7; June, 6; July, 7; August, 11; September, 5; October, 10; November, 3; December, 4. Of 59 who developed it during the period of observation, 48 occurred between January 1 and July 1.

One thing seems certain with reference to the season and that is that excessively hot weather does not seem to play a noticeable part in causing or increasing the production of indican. June and July of last year were very hot months, and yet only 6 or 7 of these patients applied for treatment during these months.

Analyses of the cases show no particular etiological factor common to all or even a considerable number of the patients. Nearly all

of the more common forms of gastro-intestinal diseases were represented. Of the 113 patients in whom gastric analyses were made 46 showed hyperacidity, 25 subacidity or anacidity, and 42 normal figures. Whether the considerable number showing increased figures for acidity has any significance or not has not been determined. Nor do we know in how much the hyperchlorhydria is one of the causative factors and how much a result of the toxic condition. Baar found ulcer with hyperacidity to be always accompanied by excessive indican and attaches such importance to the combination of hyperacidity and indicanuria as to use it as a diagnostic sign. He says that provided ulcer of the stomach and duodenum can be excluded, hyperacidity with indicanuria indicates an extragastric lesion as appendicitis or cholecystitis. My own observations are not in accord with this view. Not more than one-third of my ulcer cases treated during the last year showed excess of indican. On the other hand, my records show a number of instances in which indican and hyperacidity were present, probably from the same cause, loss of nerve tone, and in which there has never been any suspicion of extragastric inflammatory trouble.

Uncomplicated constipation does not seem to be instrumental in causing indicanuria, although a few observers have noted a considerable excess of indican in a majority of their patients with chronic constipation. Only a small number of my patients seeking relief for chronic constipation showed indican in excess. The condition of the bowels in my series was as follows: Constipation, 60; looseness, 15; constipation alternating with diarrhea, 13; and the balance normal. Many are classed with those having constipation who are merely of the constipated tendency, some of them having daily bowel movements unaided most of the time, others having daily movements, with the aid of medicine, while some were obstinately constipated. Several of the patients with the most persistent and marked indicanuria came in the class of those having normal daily bowel movements. At all events, it is a question whether the condition of the bowels should be discussed under etiology or symptomatology, as it is more than likely that a considerable part of the constipation or diarrhea may be the result of the intoxication and not one of its causes.

Obstipation resulting from obstruction of the transverse colon or above it can result in profound indicanuria, but this diminishes as the obstruction is lower down and affections of the lower part of the gut are only exceptionally complicated by indicanuria.

Although not represented in my series, it is well known that indican is greatly increased in peritonitis, typhoid, and cholera. Also occasionally responsible are ozena, caries, and other pus collections. Baar has found that after all operations in which the intestinal wall was cut or the organs roughly handled indican was present in the urine for a week.

Although some observers have claimed that affections of the liver are frequently productive of indicanuria, the writer is still of the opinion previously expressed, that the indicanuria is a complication and not a direct result unless in case of extreme hepatic insufficiency.

Probably the most frequent cause of the putrefaction resulting in indicanuria, according to the writer's opinion, is a combination of improper diet—most often excessive quantity—and a run-down condition with loss of nerve tone. As has been mentioned, this fact has been demonstrated by the greater number of cases encountered in Washington during the period of the year furthest from the vacation or at the end of the busy season.

Is there a symptom-complex which will enable us to say that the patient is suffering from an intoxication manifested by indicanuria? There are some who do present typical and complete clinical pictures, but the majority in my series had but a few of the symptoms. These, while not always characteristic, were usually indicative of an intoxication by a poison having especial predilection for the nervous system. Close analysis was made of the response to the question, "What symptoms trouble you most?" and then to specific questions concerning headache, dizziness, etc.

The typical symptom-complex consists of vertigo of varying degree, dull headache, languor, drowsiness, depression, lack of ambition, inability to concentrate the mind, insomnia, or sleep that is not restful, easy fatigue, irritability, gas in the bowels, muscle pain and cramps in the legs, cold hands and feet, and fetid breath. In many there was a partial loss of coördination. None of these symptoms were constant, but nearly all the cases exhibit some of them. However, a few cases had no symptoms at all. Mr. E. F., whose case will be mentioned below as illustrating another point, had indicanuria of the greatest degree almost constantly for twelve years, and yet most of the time felt in perfect health.

The one symptom which in the largest number of patients was complained of with the greatest degree of regularity was gas formation in the bowel, indicating the underlying putrefaction. Ninety-six patients were troubled with this symptom.

Early fatigue was mentioned among the most troublesome symptoms by 32. This state of tiring easily was met with in nearly all of the patients, but the routine of questions asked in my office does not include this question specifically. These 32 volunteered the information without questioning. Allied symptoms of constant languor and depression usually accompanied the fatigue, but 17 patients complained of these symptoms without noting the fact that they tired easily.

The patients were questioned specifically concerning headache and dizziness. Sixty had headache in some degree or form. Occa-

sionally the pain would be neuralgic in character, but more often a dull frontal ache. In some it occurred comparatively rarely, while in others it appeared almost daily. Frequently the pain was found to be worse in the morning.

Fifty-five patients of the series were troubled with dizziness. This also varied in character and time of appearance. In some it manifested itself merely by a transitory light-headedness. In others there would be sharp attacks while in some the vertigo would be almost constant, and so severe as to cause staggering.

The severity of the headache and dizziness as well as of the other symptoms does not seem to bear a direct relationship to the degree of indican excreted, but perhaps rather is dependent upon the tolerance of the patient for the poisons.

Insomnia was noted not infrequently. Again, often though the patient could go to sleep without any difficulty, it would not be restful or refreshing, and there would be a feeling of exhaustion in the morning.

One of the evidences of intoxication which, although it occurs comparatively rarely, seems to be quite characteristic, is pain in the legs and perhaps other muscles. There is no soreness to the touch, as a rule, but a decided pain varying from a cramp-like condition of the muscles of the calf to a steady rheumatic ache.

Other nervous symptoms noted in my series are loss of memory, uncertain feeling in the head, rush of blood to the head, inability to think while at work, lack of will power, phobias of various sorts, hazy spells during which things seem far off and veiled, feeling of panic, loss of consciousness for short period, palpitation of the heart, faintness, cold hands and feet, numbness in hands, loss of taste and smell, black specks before the eyes, free perspiration, and irregular muscle twitching in different parts of the body, occurring especially during sleep.

From the foregoing it may be seen that the toxins affect the nervous system in a variety of ways. None of the symptoms are entirely characteristic, but a combination of some of them is very suggestive, and we should be able to make a tentative diagnosis before examination of the urine. Often we are misled both ways. It not infrequently happens that in a patient with decidedly suggestive symptoms repeated examination of the urine fails to reveal excess of indican, and, on the other hand, quite marked amounts of indican are many times present without any symptoms to indicate such a state.

Examination of the patients in my series revealed, in addition to the many conditions present from accompanying disorders, some which are more or less frequently met with as a result of the intoxication itself. The skin was often found pale and dry, and various skin eruptions were not uncommon. Nearly all of the series had an anemia more or less marked, the average being about 72 per cent. hemoglobin.

Bram has recently claimed that indicanuria and albuminuria are not commonly found at the same time, and that the presence of one in considerable amount would indicate the other to be absent or in small quantities. He makes these deductions from 500 examinations at the Medico-Chirurgical and Jewish Hospitals of Philadelphia. One hundred and eighty-seven of the specimens of urine showed albumin but no indican; 210 showed indican but no albumin; 4 had albumin with a questionable trace of indican; and 2 had indican with a questionable trace of albumin.

On the other hand, Daremberg found that 95 per cent. of his patients with indicanuria had also an albuminuria. In my series it was exceedingly common to find albumin, usually in faint traces and hyaline casts indicative of a chronic interstitial change, and, indeed, it would be surprising if some change were not induced in the kidney by long-continued excretion of poisons.

One patient who had large amounts of both indican and albumin continuously presented such an interesting condition that his history will be given with some detail:

Mr. E. A. F. consulted the writer January 31, 1911. He was a newspaper man, aged thirty-one years, with a history of having had marked albuminuria and indicanuria for thirteen or fourteen years continuously. Frequent examination by competent observers indicated that the two conditions varied with each other. Most of the time he had no symptoms, even when indican and albumin were both present in large amounts, but for the previous six months he had had gas in the stomach and bowels off and on accompanied by intestinal distress and attacks of headache. His bowel actions were fairly regular, but with a tendency to looseness. He always felt worse just before the bowels moved. He also complained of indefinite pains in the calves of the legs after walking. He had no dizziness, and was always able to carry on hard work.

On examination his physical condition was apparently excellent, being negative except for a slight aortic systolic heart murmur. His blood pressure at the time of the first examination was 162 mm. Examination of the stomach contents showed increased figures, free HCl, 76; total acidity, 90. His hemoglobin, 78 per cent. The urine on first examination showed specific gravity, 1020; albumin, 6.5 per cent.; indican, plus 2; numerous hyaline and finely granular casts. His weight was 174 pounds. Throughout February daily examination of the urine was made, the indican varying from plus 1 to plus 6 and the albumin keeping pace with the indican. During the last half of the month the patient began to respond to the treatment, and the indican for a period of several weeks was either normal or but slightly increased, while the albumin sank to 1 per cent.

March 3. After harder work his indican again abruptly rose to plus 4, persisting at that figure for nearly a week, when it was



again controlled and gradually sank to normal again, then increasing correspondingly.

March 23. The effects of nerve strain in handling Congressional reports for his paper again became manifest, and the indican did not again become normal for three months, when he took his vacation. Congress remained in session unusually long during the spring of 1911, and his work was so arduous as to offset any advantages secured by the constant treatment. All symptoms had ceased after the first two weeks of treatment by hygienic measures, diet, and irrigations, and there was no return of them until the indican again increased.

During the three months of constant and severe indicanuria various methods were tried in addition to the irrigations, all without influencing the amount of indican in the slightest, although each change would give the patient a feeling of well-being. Cultures were made of the stools and an intensely acid colon bacillus was found to make up about 98 per cent. of the bacterial content of the bowel. Vaccines were administered several times. Rapid variations in the diet were made, with the object of changing the bacterial flora of the intestines. Hot baths were tried. Bile salts were administered. Finally thyroid extract was tentatively tried a few days before he went on his vacation, and apparently diminished the amount of indican considerably. While on his vacation of several months he took on his own initiative the thyroid almost constantly. On his return to the city in the fall he had lost weight, going from 174 to 144½ pounds as a result of the thyroid, but he felt fairly well. He still had some increase in indican excretion, about one-half of the amount he had before going away.

The cure for indicanuria must come through measures preventing the formation of toxins and the elimination of those already formed. In the treatment it is necessary first to eliminate if possible the primary cause of the excessive putrefaction and to prescribe treatment for any disorder of the gastro-intestinal canal whether causative or associated with the production of indican. Further consideration will not be paid to this, as it includes the treatment of nearly all of the gastro-intestinal disorders. In a not inconsiderable number of the cases the excessive production of indican ceased without direct measures being instituted for its treatment when the mental strain was removed; other cases have taxed our ability to the utmost before they have responded to treatment.

Measures directed toward the putrefaction and indicanuria itself consist of general hygienic directions, diet, exercise, irrigation, and occasional medication. Purgatives not only do not cause a diminution of the indican, but may even be followed by increased excretion. Irrigations are nearly always found necessary when direct treatment for the indicanuria is needed. Different solutions have been used to meet varying conditions in my series. Salt

solution, soda, argyrol, and ichthyol have all given admirable results. Ichthyol solutions often seem effective when others have failed.

In arranging the diet we have greatly reduced the proteid food, thereby removing much of the material available for the putrefaction. Frequent changes in diet have been tried, with the idea of producing unfavorable conditions for the growth of the putrefactive bacteria. Although buttermilk has been given to many, the writer's experience with it, and the artificial preparations of the lactic acid bacilli has not been such as to cause any reliance to be placed in these preparations *per se*.

No one point has been found to be of more importance in those many cases where overwork is a factor than a restoration of nerve tone, as by a vacation spent under ideal conditions in the mountains. Some of my patients have indicanuria which recurs with some degree of regularity in the spring, disappearing after a thorough bodily and mental rest.

In the majority of my cases cure of the condition has been comparatively easy, but in the occasional true auto-intoxication the progress has been slow and at times discouraging. Although not invariable, it has been our experience that the longer the duration of the indicanuria the greater the length of time it persists under treatment.

---

## ADENOCARCINOMA OF THE THYROID, WITH METASTASIS TO THE CERVICAL GLANDS AND PITUITARY: A CONTRIBUTION TO THE PATHOLOGY OF ABNORMAL FAT FORMATION.

BY D. J. MCCARTHY, M.D.,

PROFESSOR OF MEDICAL JURISPRUDENCE, UNIVERSITY OF PENNSYLVANIA,

AND

HOWARD T. KARSNER, M.D.,

ASSISTANT PROFESSOR OF EXPERIMENTAL MEDICINE, HARVARD UNIVERSITY.

THE underlying pathology of excessive and aberrant fat formation has in recent years been the subject of much investigation. Following the publication, in 1888, of the original article by Dercum on "Adiposis Dolorosa," many cases were placed on record as belonging to this syndrome which in the light of the newer researches into the pathology of fat formation have been segregated into other groups. The general tendency has been to divide the various pathological forms of fat formation into groups according to the clinical picture. The following clinical forms have been described: (1) Dercum's syndrome—adiposis dolorosa, (2) adiposis tuberosa

simplex (Anders), (3) symmetrical adenolipomatosis (Launois and Bensaude), (4) adipositas cerebialis (Froelich), (5) adipositas pinealis (Marburg), (6) nodular circumscribed symmetrical multiple lipomatosis, (7) adiposis secondary to true or neuropathic edema.

Cases of adiposis dolorosa are often met with and constitute a fairly definite clinical picture. Painful indurated areas in the fat tissue associated with asthenia, mental symptoms, and psychic manifestations, constitute the four cardinal symptoms. Anders separated from this group a series of cases showing indurated tumor-like masses in the fat tissue without pain or tenderness, and without asthenia or psychic manifestations.

Launois and Bensaude under the title of l'adéno-lipomatose symétrique à prédominance cervicale reported a series of cases of symmetrical fat deposits about the neck and shoulders that deserved special clinical consideration. Many similar cases had already been reported in the literature, beginning with that of Brody in 1846. Madelung, who wrote the first systematic treatise on the subject, considered the condition as a special clinical variety of lipomatosis. Launois and Bensaude, after digesting the literature, came to the conclusion that symmetrical adenolipomatosis, adenolymphocele, segmentary edema of Debove, neuropathic pseudoelephantiasis of Mathieu, and supra-clavicular pseudolipoma were not necessarily identical, but belonged, nevertheless, to the same morbid group. The adenolipomatosis cases of Launois and Bensaude were characterized by symmetrically placed diffused fat masses localized to the region of the neck, the axilla, and the trunk, and associated with asthenia, mental irritability, apathy and hypochondria, enlargement of the spleen, acceleration of the pulse, and decrease of small mononuclear cells. These fat masses even when of great size may be associated with general emaciation. Microscopic examinations of incised portions have shown the presence of large and sclerosed lymphatic glands in the fatty tissue. An increase and diminution in the size of the fat during its development has led Launois and Bensaude to consider the disease to have its origin in the lymphatic system.

In the only autopsy on record, Dieulafoy showed no lesion in the nervous system, but found cirrhosis of the liver and spleen and pancreas, tuberculosis of the peritoneum, adenomatous hypertrophy of the thyroid, with an enlarged and congested pituitary body. The fat masses showed no evidence of lymphatic tissue, and the nodules noted were evidently due to an invasion of connective tissue. Lyon includes an autopsy, reported by one of the authors of this paper with Dercum, as belonging to this group. This will be considered later.

Adiposis cerebialis. This condition described by Froelich has a very close analogy to adiposis dolorosa. In its simplest form it consists of an excessive general adiposis developing during the

course of a brain tumor, which in most cases has been found at autopsy to involve the pituitary body, but which in one case was found to involve the pineal gland (Marburg). A close association has been found in this group of cases with defective development of the genital organs. E. von Eiselberg has reported marked improvement and apparent cure after the removal of the pituitary body in 2 cases.

Nodular circumscribed symmetrical lipomatosis. Multiple isolated lipomatous tumors have occurred symmetrically placed in different portions of the body. On account of the symmetrical arrangement and on account of the association of the tumors, with tabes, general paralysis, sciatica, etc., it has been assumed that the nervous system and more particularly the trophic centres in the spinal cord were the cause of the affection. There is, however, practically no evidence to support such a theory. As many as 2000 of these lipomatoma have occurred in the same individual (Launois and Bensauode).

Adiposis secondary to true or neuropathic edema is a gradual transition and transformation of tissues which are the seat of chronic edema to at first pseudolipomatous, and later, true lipomatous tissue. Two groups may be identified: (1) Neuropathic edemas which most often give rise to the pseudolipomatous state, and according to Strübing, are closely related if not identical with the edematous swelling of adiposis dolorosa. (2) True edemas sometimes noted on the paralyzed side of hemiplegics with failing cardiac or renal function. If the patient lives sufficiently long they may become transformed into pseudolipomatous tissue, which does not pit on pressure and which has all the characteristics of subcutaneous adipose tissue.

From a clinical standpoint the above groups stand out fairly clear and distinct. It would not be a difficult matter to form new subgroups. When, however, we consider the underlying pathological factors we find for the most part somewhat similar organic changes in practically all of the above groups. In adiposis dolorosa the first group to be studied postmortem, our attention was directed to the region of the ductless glands and the generative system. In both cases upon which one of us performed the autopsy, lesions of the pituitary, the thyroid, and the sexual organs were present. Similar lesions were found by other observers. In 7 of the cases that have come to autopsy, lesions of the thyroid, consisting in atrophy, with compensatory hypertrophy, were noted in all; tumors of the pituitary were noted in 3 cases, with pathological lesions of the gland in 2 other cases. It would therefore appear that disturbance of function of the thyroid and pituitary bodies had much to do, if indeed they were not the causative factors, with the production of this one form of pathological fat. Interference with the sexual function has long been considered an

important factor in the production of excessive adipose tissue. Whether this is a direct or indirect relationship has not been fully determined. It would appear from the work of Froelich and others that the relationship is indirect, inasmuch as tumors of the pituitary not only inhibit sexual development, but also lead to excessive fat deposition.

In a case under the observation of one of us (McCarthy), a boy when aged fourteen years, weighing less than 100 pounds, during a period of three months gained 80 pounds in weight. This was followed by mental symptoms, slow mental reaction, mental hebetude, and later, from time to time, during the last ten years, of apparent mental and physical exhaustion, with at times, delusions of persecutions. The development of the sexual function was totally inhibited, the testicle remaining the size of a filbert, with absence of hair on the pubes. In this case, in addition to the above symptoms, gigantism developed, with rapid growth, after adolescence.

We have been able to trace connecting links in several of the above groups. Beginning with *adiposis dolorosa*, with the predominance of thyroidal lesions, a case reported by one of us (McCarthy) in conjunction with Dercum, represents an intermediate type between *adiposis dolorosa* and the *adiposis cerebialis* of Froelich. Clinically, the case presented a combination of *adiposis dolorosa* and a type of *adenolipomatosis* of Launois and Bensaude. The patient was a man, aged thirty-nine years. Fifteen years previous, at the age of twenty-four years, he grew excessively fat, and later exhibited symmetrical deposits about the neck and trunk which were exquisitely painful to touch. He presented a marked asthenia, and for the last five years of his life suffered from major epilepsy. The testicles were undeveloped both to gross and microscopic examination; the penis was small, and there was a scanty growth, one might almost say absence, of hair on the pubis. At the autopsy a weight of 206 pounds, in a man of 4 feet 10½ inches was recorded. In this case *adenocarcinoma* of the pituitary body, congenital enlargement of the adrenal, *telangiectatic angioma* of the spleen, and acute *parenchymatous nephritis* were found. Extensive lymphoid infiltration was present in the subcutaneous fat, and scattered here and there numbers of hemolymph glands. In the clinical picture the presence of lymphoid material in the fat tissue in this case presents a good example of *adenolipomatosis*. Inasmuch, however, as the fat tissue itself exhibited both in its development and in its morphology the presence of pain and tenderness, and since asthenia and mental symptoms, all the characteristics of *adiposis dolorosa* existed, the case belongs in this sense to Dercum's syndrome. The rapid development of the fat after an acute infection, together with failure of development of the sexual organs, in the presence of epilepsy, with a tumor of the pituitary body, brings the case within the group of *adiposis cerebialis*.

In the following case a clinical diagnosis of adenolipomatosis was made. The scarcity of autopsies in this group makes the detailed study of this case of much interest from a pathological standpoint. Metastasis of a thyroidal tumor to other portions of the body, including the pituitary, makes the case well worth recording.

The history and notes of examinations are as follows:

M. McD., white, aged fifty-seven years, born in Ireland, was admitted to the nervous wards, Philadelphia General Hospital, September 2, 1906. Careful investigation of family history reveals nothing of importance as bearing on his present condition.

His previous medical history reveals intermittent fever when aged twenty-two years. Since that time he has been in good health until the present illness. He denies ever having had syphilis or other forms of venereal disease. Alcohol was used in excess for many years.

*Present Illness.* Present trouble began in 1903. He gave up work on account of feeling of confusion in head, with some dizziness. On attempting to get out of bed the following morning he fell to the floor. He then found that his right arm and leg were completely paralyzed. He remained in bed for a period of two months, when there was sufficient return of power in the leg to enable him to move about. Since that time there has been a progressive improvement in both the arm and the leg until at the present time he is able to use both fairly freely, with, however, marked spasticity in the right leg. On admission to the hospital there was a marked enlargement of the neck. The patient is not at all certain about the beginning of this trouble, and states that it was of slow onset and had existed for some time before the stroke. He attributed it to a gradual increase of fat, and paid little attention to it.

Physical examination shows a man above normal weight, with a marked enlargement of both sides of the neck, symmetrical in distribution, which gives to the face a bloated and frog-like appearance. This enlargement appears to be due to masses of fat tissue, freely movable, and of somewhat harder consistence than fat present in this location. There is a right inguinal hernia. The lungs show no abnormal condition. The apex of the heart is in normal position; both the pulmonary and aortic second sounds are accentuated; the heart action is somewhat irregular. The nervous examination shows the station to be fair and the gait to be hemiplegic, with marked spasticity in the right leg. The left arm is normal; the right arm is spastic, with some loss of power, the grip in the right hand being diminished. Resistance to motor tests in both arms shows a fair amount of power. The legs are fairly well developed; the right leg is somewhat rigid, and shows a marked increase of the knee jerk, ankle clonus, and a positive Babinski reflex. On the left side the reflexes are normal.

There is no Babinski reflex on the left side. The Gordon paradoxical reflex is absent on both sides. The cremasteric reflex is present on both sides. Sensation is normal over the entire body. Examination of the cranial nerves shows the pupils to be equal, with prompt reaction to light, accommodation, and convergence; extraocular movements are good in all directions. The right cheek is flattened. The mouth can be drawn to the right much better than to the left. Tongue is protruded in the median line without tremor. Whistling, mastication, and swallowing are performed promptly and without difficulty.

An examination nine months later, July 1, 1907, gave the following results: Measurement of the neck at the level of the thyroid cartilage is 20 inches. There is a marked distention of the veins of the neck and the upper portion of the thorax above the third rib. The veins are about the size of a goose-quill. The head is pushed forward and the neck has the appearance of downward displacement, as the second rib may be easily mistaken for the clavicle. The enlargement of the neck is bilateral and symmetrical, and is composed of isolated freely movable tumors varying in size from a chestnut to that of a small apple. These tumor masses are now firm and not tender nor painful. The physical examination of the chest shows that the expansion is practically nil. There is dulness to percussion anteriorly an inch to either side of the sternum above the third rib. On the left side this fuses with cardiac dulness. Posteriorly there is dulness over the upper lobes of the lungs to the midscapular region. Distant vesicular breath sounds are heard over the upper lobes posteriorly. Tactile and vocal fremitus are both increased over the upper lobes posteriorly. Vocal fremitus is absent over the anterior area of dulness.

One year later (July 30, 1908), a reexamination showed the condition to remain practically the same as that above noted on the preceding examination. The following observations, however, were recorded: There is some difficulty in swallowing; the speech is muffled and husky to such a degree that it is impossible for the most part to understand what he says. There is no dyspnea or pain. There is some limitation of movement of the head, which is more marked to the right. Dupuytren's contractures have developed in both little fingers. The blood count shows: Red blood cells, 320,000; leukocytes, 7290; hemoglobin, 75 per cent. (Fleischel). The x-ray examination at this time shows the heart displaced toward the right. The lungs at the apex are not diseased, but have lost their transparency to the rays, as is often seen in youth (Kassabian). On September 4, 1908, there was a marked increase of dyspnea and the patient was removed to the infirmary. Physical examination at this time showed a marked weakness of cardiac action. There was marked loss of muscular element at the first sound,

with marked irregularity of the heart action. There were periods of tachycardia followed by periods of bradycardia. No relationship to the respiratory rhythm could be worked out. A few days later (September 10, 1908), the heart action became much weaker, with persistent tachycardia. Percussion over the anterior portion of the chest showed hyperresonance to the clavicles. Gurgling rales were heard over the larger bronchi. The patient died the following day (September 11, 1908).

The clinical diagnosis was recorded as adenolipomatosis; general arteriosclerosis; mitral regurgitation; chronic interstitial nephritis; right inguinal hernia; terminal edema of the lungs.

The Pathological Diagnosis. Malignant adenoma of thyroid, with metastasis of cervical glands; congestion and edema of lungs; cloudy swelling of myocardium, with chronic mitral valvulitis; chronic adhesive peritonitis in gall-bladder region; chronic congestion of stomach and pancreas; chronic fibrous splenitis and perisplenitis; chronic interstitial nephritis; arteriosclerosis and edema of the cerebral meninges.

The autopsy record is as follows: Body of an adult white male, about 5 feet 6 inches tall, showing a moderate fat development, particularly about the upper parts of the trunk. Muscular development fair; pupils equal, teeth poorly preserved. Neck shows the presence of a swelling which seems to be due largely to the presence of a thyroid tumor with enlarged lymph nodes of the anterior chain. Postmortem rigidity marked, lividity moderate; green discoloration of abdomen. Preliminary incision shows a moderate panniculus adiposus and pallid musculature.

Thyroid body shows marked enlargement of all three lobes particularly well marked in the lateral lobes and less so in the middle lobe. The mass is not adherent to the surrounding tissues and is easily dissected loose. The surface is coarsely nodular, and of a glistening mottled gray and green color. The consistence varies from a soft fluctuating sensation over what are apparently pea- to marble-sized cysts, to a dense firm sensation over those parts of the tumor which are the supporting fibrous elements. The cystic portions are of a green color in many places and in other places show the brown glue color so typical of colloid. The mass cuts with considerable difficulty and shows a cystic mottled cut surface from which flows a reddish-green, somewhat cloudy fluid, apparently the result of cutting through the numerous cysts containing material of the same nature. Less numerous cysts show the presence of a dark-brown homogeneous material of gelatinous consistence. The cut surface shows many heavy bands and finer fibrillæ of fibrous tissue.

Cervical lymph nodes on both sides are much enlarged; show no gross evidence of the presence of lymphoid tissue, and are apparently completely occupied by a mass similar to that found



in the thyroid body whose presence has increased the size of the individual nodes so that they measure approximately 15 x 5 or 6 mm. These are slightly adherent one to the other, but not to the surrounding tissues of the neck.

Thorax: Right pleura is smooth and glistening. No fluid in cavity.

Right lung weighs 690 grams; as it lies *in situ* it extends well over the midline and overlapping its fellow from the position of the manubrium to the level of the fifth rib; above can be seen the middle lobe of the thyroid projecting below the level of the clavicular ends; below can be seen a small triangular area of pericardium. The lung itself is voluminous, generally dark red, and shows a smooth glistening surface, cuts easily and shows a dark-red mottled cut surface from which a small amount of blood can be expressed from the upper lobe, admixed with a frothy fluid; it crepitates throughout. Bronchi are deeply injected and show slight thickening of the mucosa and adherence of a small amount of thin bloody mucus. Pulmonary artery shows a few streaks of sclerosis. The vein is normal. Peribronchial glands normal in size and deeply pigmented. The lower lobe of the lung posteriorly shows several small areas of deep color with poorly defined edges (probably hemorrhagic) and two larger areas of marked softening with a foul odor and irregular edges.

Left pleura shows dense old adhesions about the lower lobe posteriorly to the diaphragm.

Left lung weighs 1120 grams; voluminous and generally dark red in color. Pleura shows marked adhesions; over the lower lobe several punctate hemorrhages; the lobes are densely adherent. Organ cuts with ease and shows a dark-red, moist, and mottled surface from which can be expressed a large amount of frothy and salmon-colored fluid. Organ crepitates throughout. There is a small area 3 cm. in the upper lobe posteriorly where an area of consolidation is noted; this on cross-section shows a lighter color than the surrounding parts and is finely granular in appearance and shows absence of retraction in contrast to the surrounding tissue. Pulmonary vessels, bronchi, and peribronchial glands are as in the other lung.

Pericardium smooth and glistening except for an area posteriorly on the upper surface of the left ventricle where the parietal and visceral pericardium are densely adherent.

Heart is about the size of the patient's clenched fist; soft and flaccid, shows a smooth and glistening pericardium except as mentioned above. Subepicardial fat moderate in amount; muscle cuts with ease; cut surface is grayish brown in color, distinctly friable and slightly bleeding; left ventricular wall is 13 mm., left auriculoventricular orifice 11 cm., leaflets diffusely thickened, show some nodular fibrosis about the valve margins; chordæ

tendineæ show considerable adhesions and papillary apices a moderate fibrosis. Aortic orifice, 8 cm.; valve leaflets are diffusely thickened, and sinuses of Valsalva show well-marked sclerosis not involving the coronary orifices. Right ventricular wall measures, 2 mm. in thickness; right auriculoventricular orifice, 12.5 cm.; pulmonic, 7 cm.; leaflets in both normal. Ventricular cavities somewhat enlarged and show distinct flattening of columnæ carneæ. Auricular cavities normal. Coronary arteries slightly sclerosed.

Aorta: There is extensive plaque formation in aorta and thickening of intima.

Tongue basis, larynx, trachea, and esophagus normal.

Abdomen: Peritoneum smooth and glistening except the region of the gall-bladder, where there is well-marked adhesion of the liver, gall-bladder, duodenum, and colon. The ascending colon is adherent and markedly convoluted in such a fashion that the cecum lies in the right hypochondriac region with its tip about 5 cm. below the costal margin. Appendix points down and in, slightly adherent.

Spleen weighs 120 grams; shows chronic fibrous splenitis and perisplenitis.

Adrenals. Normal.

Kidneys show chronic interstitial nephritis. Bladder and ureters, normal.

Liver weighs 1460 grams; measures, 25 x 18 x 7 cm.; firm; normal shape except for a small anteroposterior fissure on upper surface. On anterior margin there is an irregular circular area 1.5 cm. in diameter, yellow colored, with a depressed centre which on cross-section is firm, resistant, and grayish yellow, hyalin in appearance, with a deeper gray depressed centre. This area is sharply defined from the surrounding tissue and apparently replaces the liver parenchyma. Organ cuts easily and shows a bulging, profusely bleeding, generally reddish-brown surface. Closer examination shows depressed red brown central areas fusing, and surrounded by a lighter, grayish-brown peripheral area.

Gall-bladder is densely adherent to surrounding parts; no marked thickening of wall; filled with cloudy, slightly thickened, viscid bile. Mucosa normal, ducts patulous.

Pancreas shows chronic congestion.

Stomach shows slight chronic hypertrophic gastritis.

Small intestine shows slight congestion and submucous hemorrhagic points, especially in the ileum.

Large intestine approximately normal. Appendix is 10 cm. in length, patulous, and except for slight adhesion is normal.

Histological examination was made of the organs indicated in the following report:

Thyroid gland (tumor): Eight sections show an irregular mass of supporting fibrous tissue, which in places is thick and shows

definite hyalinization. A lymphocytic infiltration of variable degree is noted in nearly all the sections. Vascularization is moderately rich. The epithelium for the most part is arranged in variously sized cysts, in some sections singly, occupying almost the entire area, and in others forming minute acini whose lining wall is made up of a single layer of a dozen cuboidal cells and present in almost every conceivable grade between the extremes. These cystic areas contain an eosinophilic, structureless, and homogeneous mass with edges showing some "scalloping" toward the epithelium, evidently from this and the gross appearance being colloid. The walls of the cysts show in places distinct outgrowths into the lumina of papillæ covered with the single layer of cuboidal epithelium and having a form varying from a simple finger-like projection to villi whose subdivisions and tree-like branchings are innumerable. The supporting connective tissue of these villi is slightly vascularized and loosely arranged, the cells showing moderately large vesicular nuclei. Definite penetration of the basement membrane is to be seen in only a few instances, but small collections of epithelial cells without definite arrangement and without any evidence of basement membrane are numerous and usually lie in fairly close relation to an acinus. Throughout the tumor, lying in colloid masses, in the heart of epithelial masses, in the supporting substance of the papillæ, and well out in the larger masses of hyalinized connective tissue, are moderately numerous somewhat broken, generally rounded masses of an intensely basophilic homogeneous material which has the histological appearance of a calcareous deposit. Although this is partly deposited as an irregular mass, yet there are considerable numbers of small bodies intermingled whose lamination, globular shape, and somewhat less basophilia give the typical appearance of psammoma bodies. Diagnosis: Papilliferous-cyst-adeno-psammocarcinoma of thyroid.

**Cervical Lymph Node.** The section shows a definitely thickened capsule, underlying which are a few lymphoid cells lying between fibrillæ of dense connective tissue. The body of the node, however, shows a mass practically identical with the primary tumor, and showing both colloid and psammoma body formation; evidently a metastasis from the primary tumor in the thyroid.

**Lung:** Three sections examined. The first two sections are much alike and show extending throughout almost all the section marked thinning of the alveolar walls, with rupture so as to bring about the fusion of several smaller alveoli, with the production of a larger one. Even these thinned walls show capillaries crowded with erythrocytes and an occasional leukocyte. This congestion extends throughout the section and shows itself markedly in the larger vessels of both venous and arterial type. While the emphysema is universal, many of the alveoli are filled with an exudate

consisting in many places of a dense network of fibrin enmeshing great numbers of erythrocytes, a few desquamated epithelial cells and some coal-carrying phagocytes. A moderate amount of nuclear fragmentation is present in all the alveoli. The bloodvessels and bronchi show no notable changes, except that there is well-marked dilatation of the perivascular lymph spaces about some of the larger bloodvessels. The third section of lung shows a large amount of pneumonic exudate of the same type, there being added to it a loss of outline of the alveolar walls and a fusion of the erythrocytes in the capillaries without any demonstrable nuclear fragmentation in these parts. There is also a marked edema in association with the pneumonia in this section, showing a clear structureless material taking a slightly acid stain. Occupying a position well within the consolidated mass is a generally circular, non-encapsulated mass of cuboidal epithelial cells arranged in the form of small acini from the walls of which project compound villous fibrous tissue columns supporting a single layer of the same cuboidal epithelium. On three sides small finger-like masses of epithelium not definitely papillary, push out into the lung tissue. In two places within the tumor definite psammoma bodies are seen. Several are seen lying without the well-defined zone of tumor. Diagnosis: Passive congestion and fibrinous bronchopneumonia, with metastasis of primary tumor in thyroid.

Liver: Two sections examined. The first section shows a normally thick capsule. The capsule of Glisson, however, shows a moderate fibrosis, the elements being chiefly old connective tissue with the admixture of a few lymphocytes. The parenchymatous cells show blurring of the cell outlines and slight granularity of the protoplasm. The central vein is packed with blood corpuscles, the congestion extending out into the capillaries almost to the Glissonian capsule and producing centrally considerable capillary dilatation. No definite fibrosis about the central vein. The second section of liver shows a large area made up partly of necrotic masses infiltrated with fibrous tissue poor in nuclei, these latter, however, being distinctly vesicular in type. About the central small irregular necrotic areas are grouped a few epithelioid cells followed by a somewhat thicker layer of small round cells. Throughout these layers a rich fibrous network runs. Vascularization is particularly rich penetrating well into the zone of epithelioid cells. The walls of these vessels are of about normal thickness, but examination of the arterial walls in the capsule of Glisson of neighboring parts shows distinct although moderate thickening apparently of the middle coat of the arterial walls. A section of this part of the liver was stained for tubercle bacilli after the malachite-green method of Rosenberger, with a negative result. Diagnosis: Slight perilobular fibrosis, cloudy swelling, passive congestion, and gumma of liver.

Pancreas: Chronic interstitial pancreatitis.

Spleen: Chronic interstitial splenitis, with passive congestion.

Kidney: Chronic interstitial nephritis, with arteriosclerosis.

Adrenal: Capsule considerably thickened and the vessels overlying the capsule show marked thickening of the intima. The interstitial tissue lying between the cell groups shows moderate overgrowth. A few of the circular cell groups immediately underlying the capsule show well-stained cells which, however, are apparently fused together, distinctly granular, and show more or less nuclear obscuration. The cells of the cortical chains show well-stained, sharply outlined nuclei, but the protoplasm of these cells shows markedly the presence of numerous small vacuoles. In some situations the vacuolization of the cells is not so marked, and the protoplasm shows a distinct eosinophilia. Still other cells lying somewhat centrally show the presence of fine brown granules which occupy almost the entire protoplasm and in many cases markedly obscure the nuclei. The medulla has apparently dropped out of the section so that it cannot be described. Diagnosis: Postmortem digestion of adrenal.

The pathological examination of the nervous system showed the following:

Gross examination: The pituitary body grossly is of normal size. Its posterior half is completely changed to a multiple cystic state, with trabeculae between the cysts, and containing a colloid material, identical in color, consistence, and transparency with that of the thyroid and surrounding growths.

In the upper third of the pons there is an old thrombotic cyst, 2 mm. in diameter, just to the left of the median line, and immediately ventral to the median lemniscus. There is an extensive area of cortical softening,  $4 \times 2\frac{1}{2}$  cm., which is scooped out to the extent of 1 cm., and affects the under surface of the occipital lobe at its extreme posterior portion. Sclerosed vessels are seen in the meninges which cover this area, intact. The cortical vessels show marked arteriosclerosis. There is no atrophy; marked passive congestion and moderate edema are present over the frontal lobe. At the base of the brain the vessels show a very extensive grade of arteriosclerosis and marked tortuosity of the vessels. Both vertebral arteries make almost a complete semicircle spreading from the medulla far out toward the cerebellum. On the left side this has produced a marked kinking of the posterior cerebellar artery. The misplaced portion of the left vertebral artery has caught the tenth nerve in such a way as to fold it. It must have influenced its function by pressure. The third nerve appears to be larger on the left side than on the right, where it is also large. The infundibulum seems to be larger than it ought to be.

The pineal gland appears to be normal. The ventricles are normal. There are multiple areas of thrombotic softening scattered

through the optic thalamus, the caudate nucleus and the lenticular nucleus. One of the areas is about 4 mm. in diameter and is directly in the internal capsule of the right side. The choroids appear to be normal. There is a slight amount of gelatinous material in the posterior horns. The cerebellum appears to be normal. The spinal cord shows a few small calcified plaques over the second lumbar segment.

**MICROSCOPIC EXAMINATION.** The spinal cord apart from a few cells, showing chromatolysis, shows a normal condition. A section of the cortex shows marked pigmentation of the cells of the paracentral globule and the pyramidal cells of the motor cortex. The pigment is of the yellow granular variety, somewhat similar to that seen in senile and presenile changes. The other cells of the cortex do not show this change. The basal ganglia, pons, and medulla are normal.

**Pituitary Body:** The microscopic examination of the pituitary body shows the general picture of adenocarcinoma. The cells are columnar in type and arranged in long acini. They have broken through the basement membrane and appear in nests of cubical and irregular type of cells. At the periphery of one of the acini, there is an accumulation of the small, irregular, neuroglia type of cell, similar to that seen in the posterior part of the gland. The acini are filled for the most part with a gelatinous material, reddish brown in color, composed of some red blood cells, hyaline material, and large plasmoid cells containing bright yellow pigment. The structure of this portion of the tumor is almost identical with that seen in the primary and secondary thyroid tumors. In the posterior portion of the pituitary body the blood sinuses are markedly distended. There are foci where the small round nuclei are so markedly distended as to give under the microscope somewhat the appearance of splenic pulp. In a reticular fat tissue surrounding the posterior portion of the pituitary body, there is an accumulation of the same type of nuclei, presenting the appearance of lymphoid infiltration, very similar to that described under hemolymph infiltration of the fat tissue in the case of *adiposis dolorosa* with tumor of the pituitary body.

In the reticular structure of the anterior portion of the gland, irregular concentric bodies of calcification resembling those seen in the choroid plexus, are seen.

Sections of the pneumogastric nerve show no changes.

While the diagnosis of symmetrical adenolipomatosis according to the description of Launois and Bensaude was not borne out by the autopsy, a new pathological form of fat formation was developed associated with multiple adenoma and adenocarcinoma. This term is to a certain extent a misnomer, the condition in the strict sense of the term being more of a lympholipoma than an adenolipomatosis.

The value of this case, however, is not so much in the support of a clinical syndrome of adenolipomatosis, but rather in the bearing which diseases of the pituitary and thyroid bear to the pathological fat syndrome. A compensatory reaction has been claimed and to a certain extent demonstrated between the functions of the pituitary and thyroid. No case, as far as we have been able to determine, has been placed upon record in which a simultaneous development of the same pathological process in these two organs has been found. It is impossible to determine from the lesions of these two organs as to which was primary. It may be assumed that on account of extensive involvement of the thyroid and the metastasis to the surrounding tissues, that this was the primary lesion and that the lesion to the pituitary was secondary. This could hardly be considered in the nature of a true metastasis, and would appear to us to be the result of a compensatory overaction on the part of the anterior portion of the pituitary followed by a degenerative process predetermined in its nature by an already existing similar condition in the thyroid and surrounding tissue. The relationship of diseases of the pituitary, and the thyroid to pathological fat formation has already been mentioned. This case links together three of the groups of pathological fat: The adiposis cerebialis, adiposis symmetrical lipomatosis, and adiposis dolorosa.

The adrenals in this case were normal both to gross and microscopic examination. In some cases of pituitary lesion the adrenals have been found diseased. In a case of adiposis dolorosa with adenocarcinoma of the pituitary, seen by one of us (McCarthy), marked hypertrophy of the adrenal was present.

The relation of the chromaffin system to the function of the thyroid has already received considerable mention in the literature. Not only in this case but in a series of control cases of pituitaries from other cases; chromaffin cells could be easily demonstrated in the posterior portion of the pituitary gland (McCarthy). These cells have nothing to do with the chromophil cells of the anterior portion of the pituitary. The chromaffin cells in the posterior portion of the pituitary follow the same staining reaction as this type of cell elsewhere in the chromaffin system, and more particularly in the adrenal and semilunar ganglia. The cells show their affinity for the chrome salts in a positive manner and the chromaffin granules are best seen in unstained sections after hardening with the chrome solution. The chromaffin cells in this case did not show any variation either as to size or structure or number from those in the control cases.

## SOFTENING OF THE SPINAL CORD IN A SYPHILITIC AFTER AN INJECTION OF SALVARSAN.

BY LEO NEWMARK, M.D.,

SAN FRANCISCO, CAL.

THIS is mainly an anatomical supplement to a purely clinical account which Dr. Victor G. Vecki has published<sup>1</sup> of a young man who became paralyzed in the lower extremities after an injection of salvarsan.

Dr. Vecki relates that the patient, who was aged twenty-three years, had received at the hands of another physician from June 1 to September 3, 1908, a series of intramuscular injections of corrosive sublimate for a syphilitic roseola which had followed upon a typical indurated ulcer. On March 24, 1910, Dr. Vecki, discovering a cutaneous syphilid and extensive adenitis, treated him again with injections of bichloride of mercury. These were repeated on six successive days; then, instead of them, he was given two injections of salicylate of mercury, a week intervening between these. After this the patient did not return until May 30, 1911. It is not clear why he did come back. Dr. Vecki writes that, with the exception of swollen glands, there were no manifestations of syphilis at that time. He makes no mention of a Wassermann test. However, on June 10, at noon, 0.3 gram salvarsan was injected into each buttock. On the evening of June 12, having felt perfectly well in the intervening fifty-six hours, the man first felt a numbness in his legs, then great fatigue in them, and soon after had difficulty in urinating. Throughout the day of June 13 his condition grew worse until the power of motion in his lower extremities was almost abolished and sensibility was impaired below the level of the navel. By June 14 the paraplegia was complete in every respect.

I saw the patient with Dr. Vecki and Dr. Krotoszyner four times between June 24 and July 20, 1911. His paralysis was very flaccid. The knee jerks, at first faint and hard to elicit, after a few days became a little more active, then again sluggish, and finally, very feeble again, the presence of the right one being at first and at last quite doubtful. The heel reflex could not be obtained at any time. The plantar reflex, which at the first examination could not be provoked at all, later reappeared as an extensor response and continued so. There was no abdominal reflex. The upper border of the region of altered sensibility was irregular, tactile hypoaesthesia beginning in front at about the seventh rib on the right side and on the left at the level of the umbilicus. The

<sup>1</sup> California State Jour. of Med., May, 1912,



dulness of sensation shaded downward into profound anesthesia. Sensibility to thermic and painful stimuli was affected up to somewhat lower levels. The patient's condition precluded an exact determination of the upward extension of the anesthetics. His bladder and rectum were completely paralyzed, he had numerous bed sores and other trophic disorders, and much fever. Neither mercury nor iodid nor an intravenous injection of 0.6 gram salvarsan had any influence on his state and he succumbed August 29, 1911.

With the assistance of Dr. W. F. Beerman the spinal cord was cut up and the sections stained in the Neuropathological Laboratory of the San Francisco Polyclinic.

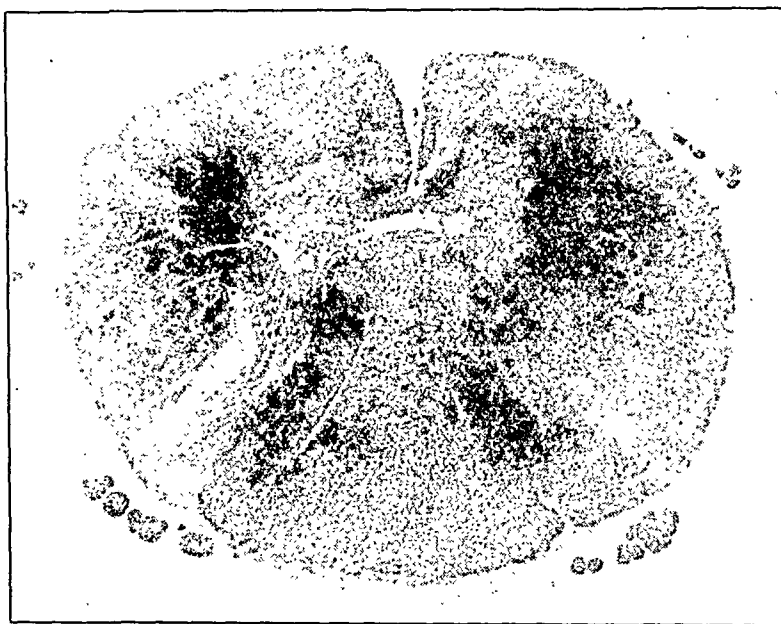


FIG. 1.—Section at upper level of softening, showing involvement of the postero-lateral region, and the anterior column on both sides, while the antero-lateral area is involved on one side only.

**PATHOLOGICAL ANATOMY.** Weigert's stain for the myelin sheath shows disintegration of the myelin and softening of the cord in the fourth and fifth thoracic segments. The destruction is nowhere quite symmetrical. At the upper level of the softening the postero-lateral region (containing the crossed pyramidal tracts) is affected on both sides, and so is the anterior column, but the antero-lateral area is involved only on one side (Fig. 1). Then in a section a little lower only a small area of myelin degeneration is found in the antero-lateral column of one side. This is followed by the destruction of nearly all the myelin on one side from the postero-lateral region forward to the anterior column, while on the other side of the cord the affection of the myelin is limited to

a small focus at the ventro-median corner of the anterior column (Fig. 2). At a distance of about 5 mm. below the section shown in Fig. 2, the disease becomes nearly symmetrical; ventralward from

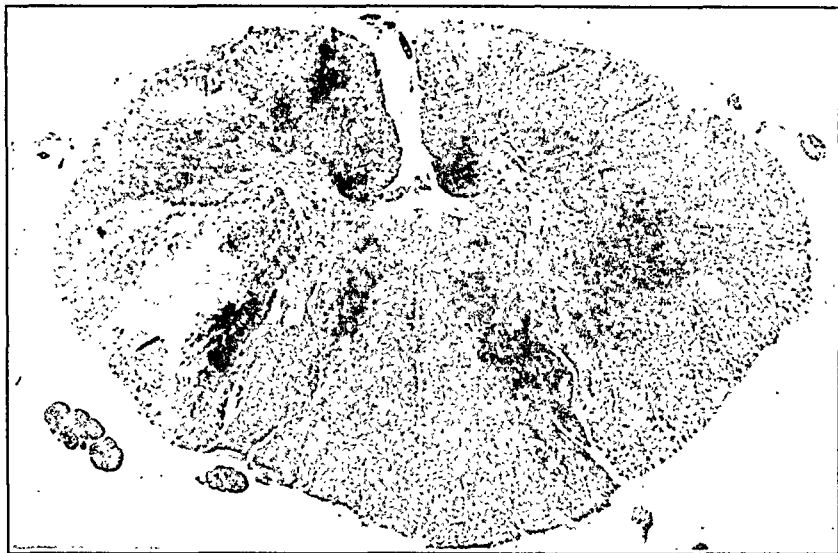


FIG. 2.—This section shows destruction of nearly all the myelin on one side from the postero-lateral region forward.



FIG. 3.—In this section of cord the disease is nearly symmetrical. In both postero-lateral areas softening has resulted in cavity formation.

the posterior horns it now spares only the white matter adjacent to the anterior horns; in both postero-lateral areas the softening of the cord has resulted in the formation of cavities (Fig. 3). Con-

tinuing the descent two small symmetrical foci of myelinic degeneration are found at the dorsal periphery of the columns of Goll next to the posterior median septum in a section which differs otherwise principally in the absence of perforations from that last described; and finally, there is a cavity again in the posterolateral region, but only one on one side.

The process of breaking up of the myelin is evidently a recent one. The fragments of myelin form bodies of various sizes, ranging from large irregular masses, and drops, down to dust-like granules, either free or contained in large round cells, the granule cells.

The morbid change is more advanced in the posterolateral columns than in the anterior. The perforation of the section is not observed in the latter. The Van Gieson method enables one to trace the steps in the dissolution of the tissue. There is, for instance, a focus in one anterior column in which the disappearance of the myelin sheath is the most conspicuous result of the disease; many axis cylinders have also disappeared, those which remain are naked; the neuroglia still persists, and in its meshes is a good deal of amorphous or finely granular material. In another focus, in the opposite anterior column, the neuroglia is vanishing, one can see neuroglial fibers break off after entering the focus from the surrounding tissue. Dorsalward in the lateral columns the tissue takes less and less of the stain, large, faintly stained, round bodies (granule cells) become more numerous, there is but a trace of the neuroglia and finally this disappears in the necrosis and liquefaction of the substance of the cord in the postero-lateral region. Nowhere is any tendency to repair visible.

The gray matter shows no loss of nerve fibers. There is congestion here and there as shown by the numerous vessels engorged with blood and by occasional hemorrhages. Not only in the gray matter within the segments which show softening, but also in other parts of the cord more or less perivascular infiltration with round cells may be seen. This is also the case in the white substance, and in one place in the column of Goll, between the seventh and eighth thoracic segments, the accumulation of round cells about two capillary vessels filled with blood has assumed such proportions as to be discernible to the naked eye in the form of a speck in the mounted section (Fig. 4). This section was submitted to Professor Ophlüs, of Stanford University, and his opinion requested as to whether this formation could be regarded as a miliary gumma. He declined to apply that term to it himself, but allowed that some pathologists would probably so-call it.

The meninges are in many parts normal, or but moderately thickened, with proliferation of round cells only in a few places; but at one spot, at the lateral periphery of the cord, near an area of extreme softening the pia mater is very much thickened and infiltrated. At this place some of the dura mater is comprised

in the section, and accumulations of round cells are found in the subdural fat.

In some sections the thickened pia closes the opening into the anterior sulcus, and the pia which dips into this sulcus often exhibits proliferation of round cells.

In the softened areas of the cord, bloodvessels with more or less thickened walls may be seen, but the most conspicuous vascular changes are observed in the pia-arachnoid throughout the whole length of the cord, being by no means confined to the softened segments. There are vessels which are thickened in all their coats

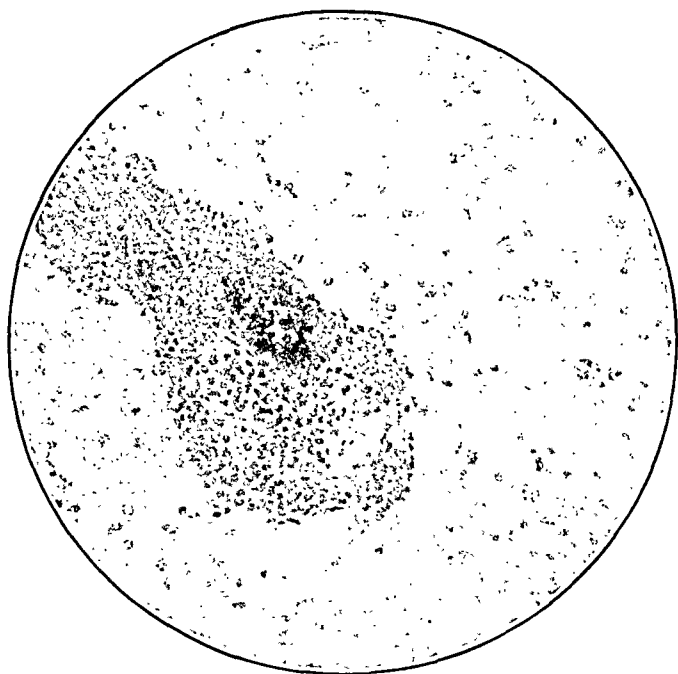


FIG. 4.—Section of cord between the seventh and eighth thoracic segments, showing accumulation of round cells about two capillary vessels.

and are completely obliterated, and now form round solid bodies of wavy connective tissue with a moderate amount of round-cell infiltration. In others the lumen is clogged by the proliferated endothelium and the wall of the vessel is thickened. In many a very small opening remains which contains blood corpuscles. The elastica of the diseased vessels does not show the resistance so often pointed out in illustrations of the syphilitic changes in arteries and veins. Weigert's elastica stain demonstrates that it is severely affected; it is distended, sometimes irregularly, or split, or broken up, and often, if at all visible, its faint fragments can be detected only when highly magnified and they remind one then of the brittle remains of worn-out rubber bands. There

is a very sharp contrast between these vessels and the numerous vessels adjoining or surrounding them which exhibit a deeply



FIG. 5.—At the bottom of this section a normal meningeal artery is shown, and above it an occluded vessel.

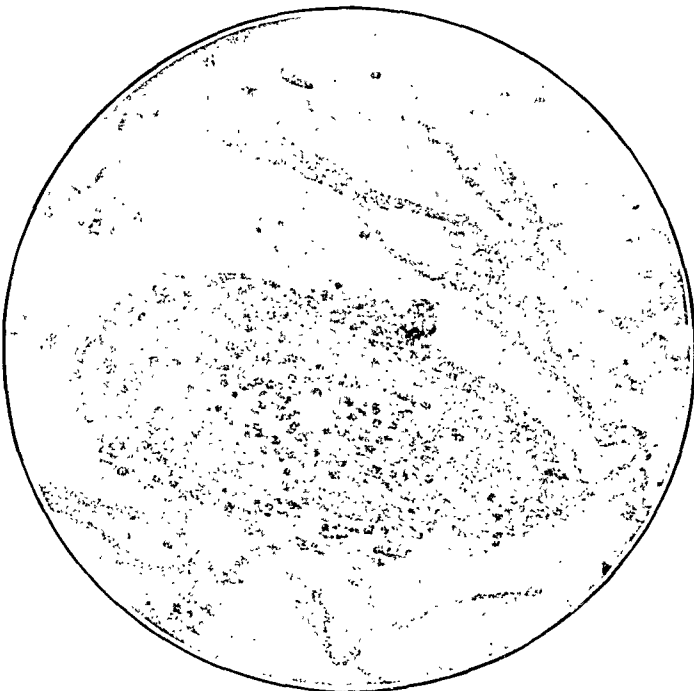


FIG. 6.—The occluded vessel seen in Fig. 5 under higher magnification.

stained normal elastica and also in other respects appear normal. These normal vessels are nearly all arteries, normal veins are far less common, and there is much reason to assume that the diseased vessels are mainly veins. Fig. 5 shows (at the bottom) a normal meningeal artery and above it an occluded vessel. Fig. 6 shows the occluded vessel under a higher magnification. The photographs are of a Van Gieson section adjacent to the Weigert section shown in Fig. 2. The vascular changes are found generally more in the dorsal part of the membranes than in that surrounding the cord on its lateral and ventral aspects, but in the lumbar region some ventral and lateral vessels are usually affected. No changes were seen in the membranes which cover the medulla oblongata.

Moderate secondary degeneration is detected by Weigert's myelin stain and also by the Marchi method in the columns of Goll and of Gowers and in the direct cerebellar tract; secondary descending degeneration in the pyramidal tracts does not appear at all in the Weigert hematoxylin sections, and in the Marchi specimens in only a very slight degree.

The gist of the foregoing is that a man who had been infected with syphilis three years before, presented the first symptoms of a fatal softening of the cord fifty-six hours after an injection of salvarsan. Was the salvarsan in any way to blame for the condition which followed its injection?

Samuel Johnson wrote more than one hundred and fifty years ago: "It is incident to physicians, I am afraid, beyond all other men to mistake subsequence for consequence." The problem of discriminating between *post hoc* and *propter hoc* continues to haunt us with all its perplexities, and in the case before us it is exemplified anew.

It is the rather close sequence of drug and disaster that impresses us with a sense of cause and effect. But opposed to the assumption of such a relation there is the clinical knowledge that acute syphilitic spinal paralysis occurred not uncommonly within three years after the infection before the introduction of salvarsan. Moreover, regarding the case from the anatomical side, it may be confidently asserted that a pathologist who might examine the specimens in this case, upon seeing the softening, the localized meningitis, the perivascular infiltration, and the widely disseminated vascular occlusions would first inquire after syphilis as an etiological factor, and, finding it, would have no occasion to seek farther. Thus clinically and anatomically the evidence in favor of the sufficiency of syphilis to produce the disease of the cord seems complete, and there would appear to be no room for the intervention of salvarsan. Even the argument which would still insist upon the striking order of events might be met, with a semblance of refutation, by an appeal to records of cases in which signs of serious damage to the central nervous system have super-

vened upon an injection of mercury. Thus a patient of Collins and Taylor,<sup>2</sup> who had had previously no sign of disease of the brain or cord, received one day, about six months after infection, an injection of mercury, felt the next day a numbness in the right leg, which he attributed to the injection, and at the end of a few days was paraplegic.

Of course, long use of mercury has taught us that no such effects are to be apprehended from it. But the comparatively brief experience with salvarsan has not permitted such a sense of security. A growing list of affections of the cranial nerves, the brain, or the spinal cord, subsequent to the administration of salvarsan will not let the suspicion die that we have to deal with a consequence of the remedy. Consider, for instance, the case reported by A. Westphal<sup>3</sup> of a tabetic woman who died seven hours after an intramuscular injection of 0.4 gram of salvarsan. The postmortem examination showed syphilitic changes in the cervical cord and in the cervical anterior roots which contain fibers of the phrenic nerve. Take, furthermore, the case reported by Juliusberg and Oppenheim<sup>4</sup> whose patient received two intravenous injections of salvarsan, each of 0.4 gram within six days, about three months after the infection, while the primary lesion was still present and swarming with spirochetes. Four days after the second injection this patient was seized with spastic paresis of the lower extremities, disturbance of sensibility, and complete paralysis of the bladder and rectum. As improvement ensued upon the treatment with mercury and iodid it was concluded that the disease of the cord was syphilitic.

When subsequences repeat themselves with some degree of uniformity they come to be looked upon as consequences. Hence that which with good reason might be interpreted in Dr. Vecki's case as a mere coincidence, when this case is considered by itself, assumes in conjunction with other similar observations the importance of a consequence. It must, therefore, be admitted after all that the salvarsan was somehow an agent in the final result.

The Herxheimer reaction has been adduced to explain such effects of salvarsan. The symptoms are supposed to be produced by a reaction in syphilitic tissue; syphilis seems to be indispensable for such action of salvarsan as we are considering. The drug appears to have a determining or precipitating or energizing influence upon syphilitic processes, perhaps identical with the influence upon which its remedial action depends. But there seems to be little or no reason to apprehend a direct noxious operation upon nervous tissue unaffected by syphilis. In this connection I may mention that in some cases of tumor of the brain and

<sup>2</sup> AMER. JOUR. MED. SCI., 1909, cxxxvii, 216.

<sup>3</sup> Berlin. klin. Woch., 1911, xxviii, 976.

<sup>4</sup> Münch. med. Woch., 1911, lviii, 1558.

in the spinal canal under my observation, which owing to a misleading positive Wassermann reaction were treated with salvarsan, no deleterious results occurred, although the cases are too few to impart the confidence derivable from a larger number. Moreover, F. Epstein,<sup>5</sup> in the course of a discussion of the effects of salvarsan upon the eye, refers to the absence of nervous disturbances in the many patients who have been treated with salvarsan for malaria and other non-luetic diseases, and he quotes especially a report on 700 cases of *frambœsia tropica* in which no mention is made of any injury to the nervous system.

To Dr. D'Arcy Power, of the San Francisco Polyclinic, I am indebted for his kindness in photographing the microscopic sections.

---

## BANTI'S DISEASE AND ALLIED CONDITIONS.

BY RICHARD STEIN, M.D.,

VISITING PHYSICIAN TO THE GERMAN AND THE LEBANON HOSPITALS, NEW YORK.

As a result of nearly thirty years' study, Banti,<sup>1</sup> a Florentine pathologist, recorded his investigations in a recent paper, summarizing his conclusions, previously published in various journals, as to the nature of the disease which bears his name. This disease, though not frequent, has called forth a deal of discussion; and any one who sets out to peruse the literature is at times bewildered if not totally discouraged, as pathologists, clinicians, and surgeons are sadly at variance as to the very existence, not to speak of the nosology, etiology, pathogenesis, and pathology of the disease. At the outset it may be stated that although it seems ill-advised to include under the name of Banti's disease any case which does not conform to the tenets set down by Banti himself, the impartial critic is bound to confess that any contribution to a subject in the making, like the one under discussion, is welcome if it is made with the requisite thoroughness of observation, so that its results may count in determining the status of a disease which, to say the least, it is difficult to delimit. It is to be deplored that many of the cases which are brought to bear on this subject are incompletely recorded, and that their pathological histology has received such scant attention. Since Osler<sup>2</sup> first drew the attention of the profession to the subject American and English clinicians have shown interest in the disease and its allied conditions.

Banti's disease is a primary splenomegaly of unknown origin;

<sup>5</sup> Berlin. klin. Woch., 1911, xlviii, 2328.

<sup>1</sup> *Folia Hæmatologica*, Part I; Archiv, x, 33. See also Ziegler's Beiträge, 1898, Band iv, p. 21.

<sup>2</sup> AMER. JOUR. MED. SCI., 1900, cxix, 54, and 1902, cxxiv, 751.



it is cryptogenetic, that is, not caused by syphilis, malaria, or leukemia. It is not a form of cirrhosis of the liver, as claimed by Naunyn, but a unique morbid entity, which shows: (1) Anemia of a characteristic though somewhat variable type; (2) cirrhosis of the liver which is identical with the ordinary Laennec's interlobular fibrous form and always is secondary to the splenomegaly; (3) ascites; (4) progressive hyposthenia, which invariably leads to a fatal issue; and (5) according to Senator<sup>3</sup> and Osler, it is not infrequently accompanied by severe or fatal hemorrhages from the nose, esophagus, stomach, or bowels. A low fever is sometimes observed.

In order to satisfy the practical demands of the clinician, Banti divides the disease into three stages: The first stage, which is marked by splenomegaly and anemia alone; the second stage, in which the enlarged cirrhotic liver becomes palpable; and the third, or ascitic stage. These three stages are subject to variations in length and intensity. The ascitic stage is terminal. Banti advises removal of the spleen before ascites sets in as the only means of curing this otherwise lethal constitutional affection.

What are the anatomical characteristics of Banti's disease? An extensive proliferation of the reticulum of the spleen, styled by its author fibroadenie. By this term he means to convey the fact that the lymphatic stroma of the pulp as well as that of a large number of the follicles, retains its reticular or adenomatous appearance. These changes take place primarily around the pencillated arterial system of the follicles, leaving the arterial walls intact. This pathological change is not characteristic of Banti's disease alone, but may be found in other diseases of the lymphatic system, as in leukemia. Although this process may be viewed in the light of a fibrosis, and is generally looked upon as such by pathologists, Banti lays stress on the proliferation of the lymphatic tissue of the pulp and the follicles in contradistinction to the ordinary (fibrous) proliferation of interstitial elastic or embryonal tissue. The changes in the liver are the well-known hypertrophy of the interlobular tissue, with secondary atrophy of the liver cells. Banti has taken particular pains to prove this, by probatory excisions and punctures of the liver. Naunyn<sup>4</sup> denies this; he claims that the hepatic changes are those of a primary lymphoid periportal infiltration. According to his view no evidence has been adduced to show that true cirrhosis of the liver develops from these interstitial changes.

Aside from the changes in the spleen and liver, there is often, though not invariably found, an endophlebitis of the splenic as well as the portal vein, at the point of entry of the former. In the

<sup>3</sup> Berl. klin. Woch., 1901, No. 46, and Deutsche Klinik, 1903, iii.

<sup>4</sup> Versammlung deutscher Naturforscher, Breslau, 1904.

third or ascitic stage of the disease, endophlebitis of the mesenteric veins is not uncommon.

It has been variously stated that Banti has classified the disease under discussion as an essential disease of the blood—as a disease of the hematopoietic organs. This is according to his own estimation of the condition, aside from the facts. Senator puts down leukopenia as a constant symptom. From the exhaustive hematological studies of Banti it is apparent that the leukopenia, though often observed, is not constant. The main blood changes are: (1) The number of erythrocytes is diminished; this is not constant, erythremia even being found in some cases; (2) the color index is lowered; (3) nucleated red cells and myelocytes are never present; (4) oligochromemia is always present; (5) leukopenia is present, though not invariably.

As regards the various forms of leukocytes: (1) There is an absolute or relative mononeucleosis; (2) there is an absolute or relative neutrophile leukopenia; (3) there is an absolute lymphocytic leukopenia.

The conclusions drawn by Banti are as follows: As the lymph nodes and bone marrow show nothing abnormal, there is on the one hand no evidence to prove that blood formation is impeded. Furthermore, as there is no urinobilinuria and no blood pigment in the spleen and the liver, there is nothing to show that there is an increased disintegration of the blood. It is, therefore, likely that the various elements of the blood are not thrown into the blood stream in sufficient quantities; there is also a possibility that they are retained in the hemopoietic organs.

What is the nosological relationship of Banti's disease in the medical system? According to Banti it belongs to the group of splenic anemias, or what is the same, primary splenomegalies of unknown etiology. He is inclined to assume two varieties of splenic anemias. The first or blood-disintegrating type of splenomegaly, in which the deleterious effect of the toxins formed in the spleen is principally exerted on the blood; in these cases the prosthemic symptoms predominate, and the patient dies from the effects of the severe anemia. In the second group, the toxins give rise to cirrhogenetic changes in the spleen and later in the liver. This latter group includes the Banti of three stages: Splenomegaly, cirrhosis of the liver, and ascites.

It should be added that in various communications aside from those of Banti, enlarged lymph nodes and embryonal bone marrow are noted, as also urinobilinuria. In his latest communication Banti states that endophlebitis of the portal root branches is not constant.

From this short review it can be seen that we are dealing here with a topic of extreme interest. This much can already be said: The various attempts to overthrow or to dissociate the pathological

and clinical complex constructed by Banti have so far been unsuccessful, and the brilliant results obtained by surgical intervention will always stand. The various points in dispute, however, call for a closer study of the subject. A great deal is still to be learned as to the etiology, pathogenesis, and delimitation of Banti's disease from apparently similar groups of diseases. The whole subject, in fact, has assumed a new phase in the light of our recent advanced means of diagnosis of syphilitic disease. In order to bring out the various points at issue, it is of advantage to pass in critical review the principal work recorded in the literature of the subject.

THE TEACHINGS OF THE NAUNYN SCHOOL. As we have seen, Banti holds that the disease is a primary affection of the spleen, with secondary implication of the liver. This is a new departure in visceral pathology, for it always has been held that, aside from certain new formations of the spleen, whatever changes are found in that organ are secondary, and are caused by inflammatory conditions of those viscera, whose blood is gathered in the portal vein. This point is specially emphasized by Naunyn, who cannot agree with Banti in the interpretation of the disease. Splenomegaly with cirrhosis of the liver (Banti's disease) is, according to Naunyn, nothing more than a cirrhosis with the precirrhotic splenic tumor of Leichtenstern. Naunyn has seen cases with considerable splenic tumefaction (30 c.c. in length), anemia, ascites, and hemorrhages which are to him nothing more than forms of cirrhosis of the liver. He would relegate Banti's disease to that class of rare cases mentioned by Senator, in which ascites supervenes the splenomegaly, without the intermediate stage of cirrhosis.

Naunyn's attitude toward the whole question is upheld by Simmonds,<sup>5</sup> who states unequivocally that the diagnosis of Banti's disease cannot be made anatomically. The case recorded by Simmonds does not seem to have been studied with the completeness necessary to give sufficient ground for the sweeping statement quoted above; nor does it become clear from the short report, whether this author has observed cases of true Banti's disease.

The same criticism holds good for the observations including studies in metabolism of Umber<sup>6</sup> and of Brugsch.<sup>7</sup> Umber published a case which neither clinically nor pathologically is a true Banti. Starting from the original theory of Banti that the disease is caused by some toxin generated in the spleen, Umber determined the nitrogen balance and found evidence of toxigenic proteid disintegration. Splenectomy was done, whereupon all the symptoms disappeared, and the patient made a complete recovery. The metabolism was normal shortly after the operation. To prove the value of the metabolism test as an indication for splenec-

<sup>5</sup> Aerztl. Verein in Hamburg, 1905.

<sup>6</sup> Zeitschr. f. klin. Med., 1904, Band iv.

<sup>7</sup> Mediz. Klinik, 1905, No. 23.

tomy, Umber cites another case with hemoglobin of only 18 per cent., which seemed absolutely hopeless; fifteen punctures were done to relieve the ascites; exitus was daily expected. The nitrogen balance being normal, splenectomy was not attempted. All at once the patient improved rapidly, the ascites disappeared, and the erythrocytes were doubled in four months; but the size of the spleen remained the same. The subsequent history not being known, this improvement cannot be considered in the light of a cure. Brugsch follows closely the teachings of the above-named authors.

The teaching of Naunyn and his pupils may be summarized as follows: There is a form of cirrhosis of the liver which is accompanied by a considerable enlargement of the spleen. The interpretation put upon these cases by Banti as a primary splenomegaly cannot be upheld. Banti's disease (splenomegaly with ascites) is an extremely rare condition, which cannot be differentiated from cirrhosis with splenic engorgement. Anatomically, the diagnosis of Banti's disease is impossible to make. Splenectomy is indicated only when the toxigenic character of the case is demonstrated by the metabolic tests. Banti's disease may recover without operative interference.

THE HEMATOLOGICAL ASPECT OF BANTI'S DISEASE, AND ITS RELATION TO THE SPLENIC ANEMIAS. Banti is reserved in the interpretation of the blood changes, as well as in its classification in the medical system; he simply states that the affection probably represents one peculiar group of primary splenomegaly. According to Grawitz<sup>8</sup> it may be called a splenic pseudoleukemia, as it represents a primary adenomatous proliferation of the spleen. In this connection I would like to refer to an excellent study of Hultgen<sup>9</sup> who has constructed a short classification of the generalized primary affections of the hematopoietic system according to their essential hematology, and subdivided them according to their etiology and clinical course. Hultgen retains the name splenic anemias, a term first introduced by Griesinger, and later employed by continental authors, Osler, and others, but discarded by Naegeli.<sup>10</sup> Hultgen places Banti's disease under group *a* of his splenomegalies, that is, the group of unknown etiology, while under group *b* he places the splenic anemias of known etiology, such as the malarial, syphilitic, etc. To the latter group, in my opinion, should be appended the splenomegalies due to thrombophlebitis of the portal system. The conclusions reached by Hultgen will, for the present at least, suffice to answer the theory of Banti's disease in its hematological aspect, as variously discussed by Banti, Luce,<sup>11</sup> Naegeli, and others. To quote: "The question as to whether in splenic anemia the plastic or the lytic function of the

<sup>8</sup> Klinische Pathologie des Blutes.

<sup>10</sup> Blutkrankheiten, 1908, p. 395.

<sup>9</sup> Jour. Amer. Med. Assoc., 1911, No. 4, p. 1526.

<sup>11</sup> Mediz. Klinik, 1910, Nos. 14 and 15.

spleen are individually or jointly involved cannot be settled as yet; but the study of blood counts of reds and total leukocytes taken from 82 cases in the literature, show distinctly parallel and synchronous movements. This I can interpret not as a sign of hemolysis, but as a slower bradyplastic hematopoiesis, as a disturbance of the entire blood-forming system."

**THROMBOPHLEBITIS OF THE PORTAL AND THE SPLENIC VEINS.** As noted above, Banti mentions certain inflammatory changes in the veins of the portal system as a common though not constant feature of the disease. These changes are always secondary to the splenomegaly, and as the disease advances toward the ascitic stage the portal radicals also become affected. It is evident from these statements that endophlebitis of the portal has no direct bearing upon the etiology of the splenomegaly.

Since Banti's disease has become more generally known a number of authors have described phlebosclerosis and calcification of the portal veins in its pathological and clinical relationship to Banti's disease. A close perusal of the cases so far published undoubtedly shows that in phlebosclerosis of the portal vein and its branches we are dealing with a process etiologically and anatomically different from Banti's disease. As pointed out by Borrmann,<sup>12</sup> it is a process much like that of luetic disease of the aorta, although traumatism is repeatedly mentioned as a contributory etiological element. In a valuable study of this subject, which also includes the experimental side of the question, Warthin<sup>13</sup> lays particular stress on the part played by the phlebosclerosis of the portal veins, in producing a clinical picture so nearly identical with Banti's disease. "The whole pathological picture" of phlebosclerosis of the portal veins "points to an infective thrombophlebitis," "no matter under what head reported, splenic or portal thrombosis, splenic anemia or Banti's disease." If I do not misunderstand Warthin, he identifies all three conditions, as he considers them brought about by one cause—thrombophlebitis of the portal veins. This theory cannot hold, as long as there are cases of Banti's disease reported without the detailed affections of the veins of the portal system. As already mentioned, such cases have been reported by Banti, and although it may be true, as Warthin contends, that the examination of the portal veins at autopsy is not as complete as it should be, portal-vein obstruction is accompanied by such an abundant development of the collaterals that it cannot be easily overlooked. Primary splenomegaly with cirrhosis of the liver (Banti's disease) is an entity apart from thrombophlebitis of the portal vein.

**THE RELATION OF SYPHILIS TO BANTI'S DISEASE.** Banti in his original communication, as well as recently, positively denies, that syphilis is a factor in the etiology of the disease in question. Within

<sup>12</sup> Archiv f. klin. Medizin, Band lix.

<sup>13</sup> International Clinics, 1910, twentieth series, p. 189.

recent years the whole subject of Banti's disease has been viewed with a great deal of interest from the fact that by reason of our improved diagnostic methods of syphilitic disease we are now enabled to substantiate the observations first made by Chiari<sup>14</sup> and Marchand,<sup>15</sup> that there is a disease which may be styled syphilitic Banti's disease, or syphilitic pseudo-Banti, which bears a remarkable relationship to the disease as originally described, both clinically and pathologically. This pseudotype is also, like the true Banti, a juvenile disease, is also characterized by enormous splenic tumefaction, enlargement of the liver, inflammatory changes of the vessels of the portal system, and blood changes similar to if not identical with those in Banti's disease—leukopenia and lymphemia. Gastric and enteric hemorrhages also occur. It is not surprising that, from the similarity of the two affections, attempts have been made to identify the syphilitic form with the original Banti's disease.

Close study of the subject reveals the fact, however, that the pathology of the cases just referred to varies materially from that of Banti's disease in the syphilitic pseudotype, the main changes in spleen and liver begin and exhaust themselves in the vascular system of the affected organs. When the process is complete, it presents the fibrous deterioration of the vessels and tissues generally which is characteristic of visceral lues. Pathologically, the syphilitic type presents a true fibrosis; a proliferation of lymphatic tissue which is characteristic of Banti's disease is not apparent. In addition to this a case of true Banti with a positive Wassermann reaction has so far at least not been observed. However that may be, the fact remains that the syphilitic pseudo-Banti bears a close relationship to the disease as described by the original author.

Anyone who studies this subject critically would be led to infer that the proof of the existence of a condition so similar to Banti's disease would tend to throw some light on the perplexing problem of the etiology of the latter; and the question naturally arises in one's mind: Has not syphilis, after all, some direct bearing upon the etiology of Banti's disease? This must not be exclusively the case, if at all; may it not, possibly, develop on the basis of a devitalized organism of hereditary or acquired luetic taint, analogous to the condition known as arteriocardillary fibrosis or that which forms the basis of certain parasymphilitic systemic diseases of the nervous system? A more complete method of diagnosis of hereditary syphilis may shed some light on this subject. Therapeutically the luetic class of cases must be viewed apart by themselves.

From the above it is evident that there is still much to be learned before we arrive at a true interpretation of the disease under discussion. No earnest effort has, so far as I can see, been made,

<sup>14</sup> Präg. med. Woch., 1902, No. 24.

<sup>15</sup> Wien. med. Woch., 1902, No. 24.

aside from the work of Banti himself, to enter into a thorough study of the histopathological basis of the disease, and we are bound to take Banti's work as the standard and accept the interpretation placed by that author upon the nature of the disease, its genesis, symptoms, and treatment. This standpoint, with certain limitations, will serve as a working basis from which the teachings of Banti can be extended. It lies in the nature of the disease, that a splenotoxic influence of the blood on the tissues, must be assumed as Banti did; to make this, however, the starting point of the whole question, has not proved satisfactory. The disturbance in metabolism noted in the thoroughly investigated case of Umber cannot be made the feature from which a differential diagnosis can be established, nor does the determination of the disturbed nitrogen balance before splenectomy bear upon the question of indication for that operation, in spite of the fact, that by this means, metabolic balance is restored. It would seem, that disturbed metabolism occurs in conditions allied to Banti's disease, and it is not unlikely, that disturbances of metabolism are but phases in the course of Banti's and similar constitutional diseases. It is safe to assume with Banti, Senator, Osler, and others, that in this disease we are dealing with a splenomegaly or splenic anemia of a peculiar type. From a broad clinical point of view it is furthermore evident, that it is above all a juvenile disease, bearing the earmarks of heredity or congenital disposition. As Luce has pointed out, it most frequently develops at the time of adolescence or shortly after, when the lymphatic structures of hereditary taint are most impressionable to various degenerative influences. With the conception of the disease, as a primary affection of the lymphatic structures of the spleen, the idea that cirrhosis of the liver is the underlying cause seems wholly improbable, although it must be granted, that clinically the differentiation of Banti's disease from certain cases of cirrhosis of the liver, with considerable splenic enlargement and severe anemia as described by Hoke<sup>16</sup> and Naunyn, must be difficult, if not impossible.

A careful study of the recorded cases shows that the pathological delimitation of Banti's disease from other forms of splenomegaly and from apparently identical conditions, always assuming the Banti standard, is practicable. The Gaucher<sup>17</sup> type of splenomegaly is a distinct entity; considerable confusion is shown in the literature by confounding the two conditions. It should be stated here that there are certain carefully observed cases still unclassified which bear a relationship to the Gaucher type, and which have nothing in common with true Banti's disease.

In conclusion, the following may be said: Banti has formulated

<sup>16</sup> *Präg. med. Woch.*, 1899, Band xxiv, p. 451, and 1901, Band xxvi, p. 431.

<sup>17</sup> A. Borissowa, *Virchow's Arch.*, 1903, Band clxxii, p. 108, and Stengel, *AMER. JOUR. MED. SCI.*, 1904, clxxiii, 497.

one group of splenomegalies, that which now bears his name, leaving for further research the grouping of other splenomegalies. The important factor of etiology he has left open. It is clearly the duty of other observers not to attempt to dissociate his symptom complex, nor to designate an allied symptom complex as Banti's disease, which differs intrinsically from that described by Banti.

THE CLINICAL ASPECT OF BANTI'S DISEASE. It is not the intention of the writer to discuss the differential diagnosis of Banti's disease from its allied conditions. The reader is referred to the excellent treatise by R. Hutchison and J. C. Ledingham,<sup>18</sup> for a summary clinical picture of the splenic anemias. Brill<sup>19</sup> holds that the Gaucher type can be distinguished clinically from other types or groups.

What seems most important to me is that for clinical purposes it is at present possible, first and foremost, to divide the splenic anemias into two groups: (1) The group with the positive Wassermann reaction, and (2) the group with the negative Wassermann reaction.<sup>20</sup> This classification will *eo ipso* determine the course of treatment, not losing sight of the fact that the Wassermann reaction may prove negative in cases of syphilis. I would propose that a provocative salvarsan injection (intravenous) be made in every case. Repeated treatment with salvarsan, together with the old-style energetic antispecific treatment, will always be in order as a tentative measure, especially in view of the fact that a certain group of cases is undoubtedly due to lues congenita tarda. Not too much, however, should be expected from the antiluetic treatment, as the disease, as shown by the fibrous organic changes, has already passed into the parasymphilitic stage, which is only in part (if at all) amenable to treatment and cure by means of the remedies at present at our command.

Finally, it should be stated that splenectomy has yielded excellent results,<sup>21</sup> and that the third or ascitic stage of the disease may now be successfully treated by the combination of splenectomy and the Talma operation. Altogether it is no exaggeration to state that the work of Banti stands today as one of the most brilliant achievements of medical science.

<sup>18</sup> Splenic Anemias in Allbutt and Rolleston's System of Medicine, v, 757.

<sup>19</sup> Medical Record, March 2, 1912, p. 444.

<sup>20</sup> Neuberger, Zeitschr. f. klin. Med., 1911, p. 92, and Ridder, Charité Annalen, 35 Jahrgang, p. 193.

<sup>21</sup> According to Rehling, 8 per cent. mortality in 70 cases; see Festschrift des deutscher Hospitals, New York, 1909, p. 320. Rehling transfused before operation.



CASES OF JUVENILE PSYCHASTHENIA: TO ILLUSTRATE  
SUCCESSFUL TREATMENT.<sup>1</sup>

BY TOM A. WILLIAMS, M.B., C.M. EDIN.,

CORRESPONDING MEMBER SOCIETIES OF NEUROLOGY AND PSYCHOLOGY OF PARIS, ETC.;  
NEUROLOGIST TO EPIPHANY DISPENSARY, WASHINGTON, D. C.

DEFINITION. The conception which Janet has formed of psychasthenia is described by him in so masterly a manner as "mental uneasiness, a state of disquiet, feelings of incompleteness, without anatomical lesions." These are interpreted by him as due to the diminution of "psychological tension." Hence, the superior functions of the brain, those of correct associations of ideas and emotions, are replaced by such inferior activities as motor impulsions, such as tics, dromomania, and other motor agitations; emotionally by distress (*angoisse*) and morbid fears (*phobias*); and intellectually by mental ruminations and manias. It is the interpretation of this state by the patient of intellectual type which leads to more systematized obsessions, which it is useless to attack directly by persuasion, for they represent a much more profound cause of which they are only a last expression. Janet recognizes the likeness of this condition to that found in cerebral "neurasthenia" of the classic type and some kinds of paranoia. There are certain resemblances also to epilepsy and hysteria. He thinks the psychasthenia may be due to an intoxication or congestion, varying with the influence of infectious diseases, fatigues, and emotions in accordance with a predisposing heredity.

The syndrome which Janet calls psychasthenia had often been noticed previously and described under such names as cerebral neurasthenia, phrenasthenia, disequibrated degeneracy, and monomania. Janet's great merit is to have shown the essential identity between manifestations which appear so different. For example, he has shown that agorophobia and claustrophobia are really two variants of a state of fear which has become morbid by being inopportune and out of harmony with reality; furthermore, the states of phobia, or angst, are merely two of the manifestations which the same patient may show when suffering from psychasthenia. Motor impulsions, of which the tics are a striking example, are merely another way in which is expressed the fundamental state of "incompleteness."

In some patients neither emotional nor motor symptoms are conspicuous; but the asthenia of the psyché reveals itself by a state of intellectual doubt, by need for verification of minute details, indecision, and a feeling of difficulty in arriving at certitude regarding the reality of anything. Janet considers the last the

<sup>1</sup> Read in the Pediatric Section, Amer. Med. Assoc., Atlantic City, June, 1912.

cardinal symptom of psychasthenia, and calls it "the loss of the function of the real." Naturally, this leads to a longing for moral support, comfort, and affection, and entails a fear of being alone, or in extreme cases, sometimes the moral distress leads the patient to relieve it by artificial excitants. Work and pleasure may be employed; but too often nepenthe is sought in narcotic drugs or debauch.

PSYCHASTHENIA IN CHILDREN. The full syndrome is only possible in people of complex intellect with highly developed emotions. Hence, children can hardly show it completely. Janet, moreover, studied psychasthenia in children only retrospectively through the reminiscences of his many patients. Although he himself indicates the conditions in childhood which favor the psychasthenic state, he has not unravelled its genesis so completely as have more recent analysts of psychoneurotic persons.

All agree that the scrupulosity and over-conscientiousness which mark the psychasthenic character are the result of over-strict training ill-adapted to the need for untrammelled unfolding required for a child's proper development. The moral and religious sanctions which appeal to the adult are injurious to this development, unless they are specially adapted to a child's intelligence and needs.

This opinion, although well founded, is based upon wide observation rather than upon individual analysis of children; for I know of no psycho-analyses of young children by trained men, with the exception of one made on a five-year-old boy by Freud, which is vitiated as an experiment because the boy's mother had been analyzed by Freud and was herself permeated with his ideas, so that it is impossible to exclude the influence of these upon her child.

Thus it is particularly gratifying to be able to bring forward some observations on psychasthenic children whom I had the opportunity of analyzing. More especially is this satisfactory because recovery was obtained in each case, and best of all, this occurred without the enormous expenditure of time which is believed to be essential for reaching the curative point in a psycho-analysis. Working against time to catch a train, three-quarters of an hour sufficed in the first case, and not more than an hour was consumed in the examination of the second case. In both cases, however, the history had been previously obtained. The third case, in an older child, more complex, although not completely analyzed, was cured as a result of four interviews which averaged less than an hour each. This economy of time is only possible to one who is experienced in the technique and psychopathological data, so that he may not be led by false scents to explore by-paths without practical significance. When this capacity is attained, the method can be employed in private practice; and even dispensaries should not

be deprived of its advantages,<sup>2</sup> for there are few procedures of practical medicine in which the direct benefits are of greater value than in the restoration to economic and social capacity of the suffering psychoneurotic, who is not only a sufferer himself, but a burden to all his connections.<sup>3</sup>

**TICS FROM MONOMANIA.** CASE I.—A girl, aged eight years, an only child, was sent to a Washington sanatorium because of numerous grimaces and gestures. These led her attendants to believe she suffered from chorea, to give her large doses of arsenic, and to isolate her from her friends, while overfeeding her. At the end of a month she returned to the country, the morbid movements having ceased, but she suffered from insomnia and was unable to go to school, in the belief of the parents, because of her "nervousness," which was especially conspicuous when reading and studying was required. When she was nine years old I was asked to see her by her uncle, Dr. Perry, of Lyons Creek, Maryland, in the hope that something further could be done.

I found a well-nourished, self-contained, sensible child, without apparent shyness, overforwardness, or hyperexcitability; but she was apt to talk rather fast, and stammered now and then. I soon discovered that she was fond of play and the companionship of which she had been deprived, to compensate for which she made believe that the objects and persons of her play were real. So rigorously was she protected that the conceptions of lying and stealing were hardly clear to her. She had been strictly managed, scolded, and repressed a good deal. She was once whipped for persistent dawdling on her way home from school. She did not remember other corporal punishments. Her life, however, was not felt to be unhappy; for she was very obedient, and was not galled by the good manners expected of her. However, she wanted to grow up, hated people to call her little, and disliked the spoiling which was a tendency of her father before her sickness. Although she did not repine at staying from school, she wished to learn to read and write; but as lessons agitated and kept her awake, she employed herself in play.

The source of the movements she had made was revealed after some hesitancy. It seemed that her mother had taught her, when aged about five years, that people lived by inspiring the air and what they expired was hurtful. This thought led to a distressing compunction about the noxiousness of her breath; if it was bad it must hurt others.

Now her training had been such that to hurt others was a great offense; but not to breathe was to die. Out of this dilemma she

<sup>2</sup> See author's "Care of the Mentally Disturbed," *New York Med. Jour.*, September 29, 1912, in which is described the organization of such a hospital and dispensary.

<sup>3</sup> The basic principles upon which are founded the methods of management of cases of this kind were first set forth in the author's "Psychotherapeutics: A Symposium," in 1909, in the chapter on "Psychoprophylaxis in Childhood;" also in *Jour. Abnormal Psychol.*, June, 1909.

found a way. Hurts could be mended; when injured did not some one "kiss it better"? Could not she then kiss better her own bad breath so that it would not injure others? Accordingly she made movements of her lips, which represented the healing kiss to ward off the danger of the deadly air she expired.

Later on her discontent was augmented by scruples against the injury she did by walking upon creatures with the hard and sharp heels of her shoes. Even the planks of the floor were of the animated world, which it was wrong to destroy or injure. To assuage the distressing thought of this, compensation must be made. She found it in another legendary therapeutic procedure, the healing touch. So it became her habit, before walking over an object, to bend and touch it with her hand.

These procedures belong to the class of mental manias which Janet has called manias of expiation. In their motorial character they approach the tics, into which they gradually blend. That they had done so to some extent in this case is shown by the fact that the kissing nature of the lip movements had not been suspected.

That the movements had not developed entirely into mere symbolic vestiges of their original purpose was due to their arrest comparatively early. That they would have developed into characteristic tics<sup>4</sup> is confirmed by the distress the child suffered in overcoming them. She did so after being in the sanatorium a few days, and did it deliberately and by a hard struggle, because she wished to return home, and they had promised that she could do so if the movements ceased. It is possible that the nurse who said this had an inkling into the psychological character of the child's disorder. After she succeeded, the desire to repeat the movements quickly ceased, although she does not know that she was enlightened regarding her notions about the hurtfulness of expired air and hard heels.

Proceeding to the genesis of the insomnia and difficulty in reading and study, interrogation showed a simple mechanism. Apprehension as to their consequences was raised in the child by the attitude of the parents, whose open fear lest they should perturb the child reminded me of the procedure of the mother of the boy whose hysterical hydrophobia was precipitated by her sitting by his bed reading about rabies two weeks after he had been bitten by a supposedly mad dog.<sup>5</sup> So in this case the ostentation of their solicitude provoked in the child that which they feared.

**TREATMENT.** The explanation of these mechanisms to both parent and child was the first task, and it proved simple, for they were intelligent people. The corollary that the child was not

<sup>4</sup> The nature and diagnosis of tic is discussed by the author in the *Southern Medical Journal*, August, 1909; *Monthly Cyclopaedia*, January, 1910; *International Journal of Surgery*, August, 1910.

<sup>5</sup> Miller, *Jour. Abnor. Psy.*, 1910.

morbid except by induction was then set forth. The conclusion was that the child should resume study and return to school in the fall in every respect like an ordinary child, now that the mother and father were warned against the evil consequences of unwise solicitude, and the induction of hyperconscientiousness in matters beyond the intelligence of a young child. The result has justified expectations, the child taking part in the school life with enjoyment.

Some might explain the case as a "fear wish" reaction of the *ædipus* type in relation to father and mother. Indeed, to the exponents of the theory upon which it depends the patient's history is not without significance, and in the absence of a dream analysis they cannot be satisfied in rebuttal. The fact, however, rests that a painful complex originating at least by the fifth year had resulted in psychogenetic symptoms, and this complex depended upon a moral concept in which the sexual life seemed to play no part whatever.

This plain mechanism of fear of bodily harm from without seems to be a much more fundamental feeling, if one is to appeal to phylogeny, than is that concerning the relations with others termed sexual. Even hedonic affects occurring autochthonously in childhood, although of the same genus as that which later effloresces into sexual emotivity, do not by any means in themselves give origin to perturbations of the psyché either in childhood or later. I say in themselves, for I believe that the perverted affectivity from which arise so many obsessions, phobias, etc., is always the product of induction, if not directly and naively from without, at least by logical induction from data acquired by observation or didaction of the conventions of family and social life. The child's avidity to relate himself correctly to these, to behave as a grown up, that being of marvelous privileges, is not sufficiently realized. It makes him seize upon the most trifling detail for imitation. One of his objects is to transcend the amusement he provokes in trying. The shame he feels at the ridicule with which his attempts are so often met causes him to keep them to himself in half shame.

CASE II.—Thus in a case of which the analysis occupied over a year, and would accordingly take too long to recount, the obsessions, which were mainly sexual scruples fundamentally, had as their basis the moral and religious repressions of the patient's childhood. It was the horror and loathing of everything pertaining to the corporeal which caused the child, when aged six years, to look upon a hedonic state which used then to occur as a sinful one, which prevented even speaking of it to the mother, and which was the incentive for the repression of indulgences demanded by a most affectionate nature, for in the family all display of affection was discountenanced. It was the lurking fear of that which was awful, because unfaced and vague, but which contained inexplicable potentialities for evil, which later permeated

the patient's relations with fellow-beings to a degree which produced utter incapacity for daily life.

PREPUBERAL IMPULSIONS. CASE III.—Let me ask you to contrast on the one hand the loss of a quarter of a century of fruitful activity by this patient, the lack of good sense in whose upbringing was so late compensated for by what we have learned of psychopathology: with the immediate compensation of an entirely similar syndrome in a clergyman's child, aged ten years, whom I saw recently. One day she would be well and the next crying, feeling miserable, tired, and dizzy, with a dull headache as a result of lying in bed thinking. The preceding summer at school she had been irritable, cross, impatient, and quarrelsome with her sister. She had formerly been easy to manage and full of life and joy. Her mother was most anxious, and took pains to avoid startling or fatiguing her, and in the belief that it exhausted the child, forbade the impulsive squeezing and kissing which the child frequently desired. She had noticed that the little girl was less impulsive and irritable when having something to do, but she had been taken from school, which seemed to aggravate her nervousness.

The physical examination was negative, with the exception of a slight hyperopic astigmatism and a variable visual acuity without apparent cause (Dr. F. N. Chisholm, who referred her).

Psychically, intelligence was normal. She was timid, hyper-conscientious, and much concerned at having been reprov'd for impulsive shouting, for violent hugging of her parents, and because of some eau de cologne she took. This had really been taken by the little sister, who was punished for it. She was sometimes so unhappy and miserable that she did not want other children near her, and she was most unhappy because she was not allowed to show her affection for her father and mother, of whom she is very fond, more especially of the latter. Her dreams are rare, but she recollected one of a white-bearded man who dragged her from the bed by her hair and another of a wild animal trying to eat her. I could not at the time obtain any associations from either of these, and, indeed, I was more concerned relieving without delay the intensity of the repressions which made the child's life a burden.

A physical factor complicated the case, the child eating excessively of meats and oatmeal, and making her principal meal at night. I believed this was the initial cause<sup>6</sup> of the irritability of temper and the impulsiveness which led the overconscientious parents to repress overmuch.

TREATMENT. Mid-day dinner was prescribed, and a supper mainly of carbohydrates and fruit, after which she should not go to bed for at least an hour. On waking in the morning the child

<sup>6</sup> See author's "Diet in Nervous Disorders," New York Med. Jour., April 6, 1912; Canada Public Health Journal, June, 1912.

was instructed to make a practice of getting up and going outside instead of ruminating in bed. The parents were told to avoid nagging her about trifles, and her behavior was to be left to take care of itself at present. Her affections were to be indulged and reciprocated; she was given plenty to do, and was sent back to school in a few days. This policy resulted in complete recovery within two weeks, the child being as happy and joyous as she formerly was.

DIAGNOSIS. I considered this a prepuberal emotionalism attributable to an incorrect dietary and greatly aggravated by parental interference, well meant but entirely injudicious. This last, the psychogenetic factor of the situation, was the main pathogen of a state which might have eventually attained a gravity like that of the case with which it contrasts.

Thus the psychasthenia of this little girl was cut short long before its root branched into mental manias or before there was a hint of obsessions or phobias. It may astonish one that I include this case in the psychasthenia of Janet, as it is without the stigmata or cardinal symptoms of that disorder, if we except the impulsiveness and the inadequacy which were hardly even conscious. The justification of such a diagnosis need not, however, detain us, for it has been set forth in explanation of the case of a child, aged only two years, which I reported to the Psychological Society of Paris in 1910.<sup>7</sup>

MULTIPLE MANIAS OF EXPIATION. CASE IV.—However, in the following case the psychasthenic syndrome was in full efflorescence:

A boy, aged thirteen years, was referred by Dr. Guy Latimer, of Hyattsville, Md., because of extreme timidity, many "nervous" tricks, and an inability to concentrate his attention. The most conspicuous symptoms were an arithmomania, a mania for verification, including a "*délire de toucher*" and a "*manie du sort*," one of the forms of which was the imperative need of lying on his back on the floor at frequent intervals while dressing in the morning. These various mannerisms intermitted and replaced one another.

Analysis revealed that all were in reality expiatory penances for a jealousy of his little brother, which had already begun at the age of three years, when he asked that the baby be thrown from the window, and once banged his head on the floor while enraged. He himself had always been much petted, and he craved it. It was the reproof of an aunt which first created the shame for his jealousy and led him to make penance in these fashions. Latterly, he had been urged to cease his peculiarities, and can stop any of them when on the alert by a hard struggle. His distress at doing so, moreover, soon passes away. But his frequent absence of mind in day dreams, which he loves, interferes with his endeavors. This tendency was favored by his not having been allowed to play the

<sup>7</sup> See also Arch. of Pediat., 1910.

games of which he is fond with the boys in the neighborhood, which is a rather rough one.

This desire for expiation began when he was aged between three and four years, by thinking it was mean not to give his toys away and so he gave them all to his brother. He was told that it was naughty to be jealous, and he felt ashamed, but did not cry, but just sank into himself and said nothing. He still reproached himself. If his mother did not pet him for a week he thought she did not care for him, and so he would be unhappy.

He does not know the reason why he is jealous of his brother, for he loves him, and they do not quarrel much, even when the other cheats at play. It is in the morning and at night that he is most beset by his manias, and he feels things would go wrong night or day if he did not perform them. He declares: "I always seem to want to do something I do not want to, because I do not want to." He does not know why. He has no shame of body or sex, as he has been fully instructed. He is very religious, believing in heaven and hell, that he must be good, and feels that he ought to make himself sad because he does not like to be sad; but he is so prone to sadness that even as a baby music made him cry. So conscientious is he that he undertakes every task with too great violence, quickly becomes exhausted, and then has to fight against the dreamy tendency which supervenes.

**TREATMENT.** Having explained together the genesis of his desire for penance, we decided to concentrate attention upon only one of his manias at a time, in order to break one by one the habits he had formed, and he was to take up carpentry work in order to combat the tendency to day-dreaming. His diet was also rectified.

More and more control was soon obtained. On last hearing from him, a year later, he had taken a position, and had overcome his disabilities.

The psychogenetic factor in this case was obviously the unwise manner in which an affectionate infant's natural jealousy was reproved by over-religious relatives. The awfulness of the sin fostered the poor boy's shame thereat, and led him to the type of expiation which follows from a misapplied asceticism.

**GENETIC TYPES OF PSYCHASTHENIA: RELATION TO HYSTERIA, ETC.** Thus in its essence psychasthenia arises as a reaction of discomfort and anguish against unnatural repressions. It is psychogenic in this form; but there is perhaps another type which precedes from a general uneasiness of the body due to a toxic factor.

**CASE V.**—Such was the case of a child, aged two years, whom I saw in the dispensary at the Children's Hospital, of Washington, with Dr. Donally. Distressing howling without relation to extraneous stimuli, the eating of sand and clay, the maintaining of a large deep sore on the wrist by scratching were among the chief symptoms which betrayed her general discomfort, against which these were



morbid reactions. I interpreted them as due to what would have been shown in older people by a sentiment of incompleteness. The cause was believed to be a diet almost exclusively of strong coffee and milk since the age of three months. The case was reported in full to the Society of Psychology of Paris, and was published in *Pediatrics*, 1910.

A SYMPTOM WHICH IS USUALLY PSYCHOASTHENIC IS STAMMERING. CASE VI.—The ten-year-old son of a Washington attorney was referred in November, 1910, by Dr. Spiller, of Philadelphia, for advice regarding a stammer of two years' duration and for "general nervousness."

A brother who had formerly stammered at the same age had recovered after six months spontaneously; but the expectations of the parents that this boy's stammer also would disappear were not fulfilled. He stammered worse when tired or when intent upon speaking correctly. In play, he rarely stammered, and a sentence was never interrupted by a stammer. The boy was fidgety, especially on speaking; but his writing was not jerky. His attention was easily tired. He was not overstudious. He did not tremble. He was not constipated. He detected differences of pitch.

His chest was contracted in front, and measured during quiet speaking twenty-three and one-half inches, expanding to twenty-four and one-half inches. By forced inspiration it could reach twenty-nine and one-quarter inches. In singing he expanded to twenty-seven and one-quarter inches. The scaphoid scapula was not present.

I omit the detailed psychic examination for the sake of brevity. In short, the cause of the stammer was a common one, the dread lest he should stammer, added to or supplemented by an insufficient preliminary inspiration. The attempt to force the voice to overcome these difficulties only added to the glottic spasm, and the contortion of the muscles of forced expiration due to his apprehension.

A series of exercises in control led to his recovery in a few months. Now the treatment of this boy succeeded only by virtue of taking into due account the psychoasthenic factor in the production of his stammer; and while that was attended to, the boy remained well for several months. When a few months ago this was neglected a relapse occurred.

The fact that a disorder may be psychogenic does not identify it with hysteria, the psychogenic disorder *par excellence*. There is still much difference of opinion how we shall define hysteria; but as I see it, the essential character of the disorder is that it is induced by an idea. This may be either revived from the patient's mind by an occurrence which strikes an associating idea or it may be direct by what is regarded as suggestion. The mechanism is the same in each case, and the term suggestion is appropriate for both.<sup>8</sup>

<sup>8</sup> See *Nature of Hysteria*, Int. Clin., 1908, iii; also *AMER. JOUR. MED. SCI.*, August, 1910, VOL. 144, NO. 6.—DECEMBER, 1912. 29

The induction which results in psychasthenia, unlike that in hysteria, is indirect. The patients indeed are not suggestible, and cannot be hypnotized as can hystericals. What is induced is a general state of ashamedness, timidity, and scruple; and it is from this morbid root which spring, by psychological processes entirely natural, the train of ruminations, anxieties, morbid fears, and manias to touch, to count, to search the past or future, to explain, to verify, and repeat, to attain perfection, and the mysticism which springs from this desire. The mania to compensate, to expiate, and to make compacts with Fate, too, proceed from a feeling of unworthiness which a scrupulous person has. From this root spring also the morbid fears of objects, of situations, even of one's own thoughts and bodily functions. The anxiety neurosis is simply one of the ways in which is manifested the psychasthenic state. A full discussion of the reason for the belief in disagreement with Freud is given by Janet, but would take too long to recapitulate.

The relation of psychasthenia to tic has been indicated above. The impulsion to tic is derived from the general discomfort and nervous instability being focussed by peripheral or central irritation upon some particular part of the body or upon some action. One type of occupational dyskinesia is an interference with the action desired through an impulsive tic which takes possession of the muscles needed for the desired act. In the author's<sup>9</sup> studies of writer's and telegrapher's cramps, this is discussed at greater length.

Finally, neurasthenia must be considered. I am of those who believe it advisable to cease the use of this term, or at least to restrict it entirely to cases of abnormal fatigability which is not induced by an idea nor caused by infections or toxines, disorders of metabolism or perturbations of the internal secretions. It is certain that psychasthenic symptoms appear quite apart from fatigue, which psychasthenics can sometimes support for long periods. Hence the treatment of the disease by extranutrition, rest, or any physical procedures is in psychogenic cases both superfluous and harmful, in that it detracts attention from the real source, namely, the psyché of the patient.

FOR CORRECT TREATMENT. Proper knowledge of the constitution of the mind of the child is the only foundation upon which to build this successful therapeutics. The diagnosis into categories, such as hysteria, neurasthenia, phobia, monomania, followed by an empirical treatment, is utterly useless because not accompanied by adequate notions of the process occurring in the mind of the patient. Doctors who treat neurotic persons with such inadequate equipment will meet with even less success than do the followers

<sup>9</sup> Jour. Psych. u. Neurol., Leipzig, May, 1912; see also Jour. Abnorm. Psych., June-September, 1912.

of an unlicensed cult; for these have a conception, however erroneous, of psychological mechanisms, and it is a conception which happens to fit a certain proportion of cases, whereas the usual physician's conception fits none at all. And a neurotic who gets well under his care does so not because of his medical treatment.

Now psychological mechanisms are most pure, and hence most easily understood in children; and it is in order to appeal to pediatricists and physicians for proper study of the nervous children they see that I bring before the profession the foregoing considerations.

I should like to add that one of the reasons why pediatricists do not take more interest in neurotic children is because the books generally take this subject up in such an unsatisfactory, vague manner. Epithets rather than causal mechanisms seem their aim. My paper is an attempt to show some mechanisms at work in individual children. The analysis and therapy do not require any special ability, merely a serious study of the child's usual and unusual modes of thought. Most of us can study this upon our own children. Besides, the analysis is easier than in the adult, for a child has less complicated motives for concealments.

Psychic disorders should be observed and analyzed clinically by a scientific method essentially similar to that used in all clinical and experimental medicine. Loose general terms have no diagnostic value until conceived with definite meaning. Such an *olla podrida* as "neurasthenia" must be either restricted or abolished if progress is desired.

Of the cognomen hysteria the same may be said, unless the term is used in a definite sense like that of Babinski, "any symptom producible by suggestion." The lesson of my cases is not the cognominal diagnosis, psychasthenia, but the revelation of the mechanism of each separately, and its removal by rational measures very different from those found in any text-book of pediatrics or even neurology.

---

## THE INCIDENCE OF PURPURA IN THE COURSE OF CHRONIC PULMONARY TUBERCULOSIS.

BY JOHN M. CRUICE, A.B., M.D.,

PHYSICIAN TO THE HENRY PHIPPS INSTITUTE OF THE UNIVERSITY OF PENNSYLVANIA,  
THE WHITE HAVEN SANATORIUM, AND TO THE OUT-PATIENT DEPARTMENT OF  
ST. AGNES' HOSPITAL; INSTRUCTOR IN MEDICINE AT THE UNIVERSITY  
OF PENNSYLVANIA; FELLOW OF THE COLLEGE OF PHYSICIANS  
OF PHILADELPHIA, AND MEMBER OF THE JOHN  
MORGAN SOCIETY.

PURPURA was known to the ancients, but under this name they not only included the hemorrhages into the skin but also the

eruption of scarlet fever and measles. In 1694, Zeller, Professor of Medicine in Tübingen, gave a good description of purpura. Werlhof described it under the name of morbus maculosus, and finally, Schönlein gave it the name of peliosis, in describing what he thought was a distinct clinical entity. Rayer, in 1827, was the first to publish a case of purpura associated with tuberculosis. Louis, in 1843, mentions a tuberculous woman, who a few days before her death showed bluish spots. Since then there have been numerous other contributions to the literature on the subject.

Bensaude and Rivet,<sup>1</sup> however, in 1906, after a study of their own cases during ten years and of the cases reported in literature, have written so far the most complete monograph. They classify the cases from a clinical point of view in four categories: (1) The cases of purpura hæmorrhagica occurring in the course of miliary tuberculosis. (2) The cases of purpura hæmorrhagica occurring in the course of chronic pulmonary tuberculosis. (3) The cases of purpura hæmorrhagica occurring in the course of latent tuberculosis. (4) The cases of purpura hæmorrhagica occurring in the course of some extrapulmonary tuberculosis. In discussing the cases occurring in the course of miliary tuberculosis they say that all the cases reported in literature that have come to autopsy show that they were not caused by a primary acute miliary tuberculosis, but by an acute miliary tuberculosis occurring in the course of a chronic pulmonary tuberculosis. They themselves have never had the opportunity to observe a fatal case of purpura occurring in the course of miliary tuberculosis.

According to these authors, purpura occurring in the course of undoubted chronic pulmonary tuberculosis is much more frequent, and most commonly appears in the terminal or cachectic stage of the disease. Its most usual form is the simple purpura, the so-called cachectic purpura, but often one sees a true purpura hæmorrhagica.

They say that there is a purpura that is premonitory of tuberculosis, upon which Rendu insisted in 1890. According to Rendu a purpura situated on the dorsal region of the hands and wrists is quite a pathognomonic sign of a latent tuberculosis, especially in old persons. There is also a true pretubercular purpura hæmorrhagica, as is well shown in the case reported by Carnot, Bensaude, and Harvier.<sup>2</sup> A young woman, weakened by childbirth, and nursing for six months, grew thin for three weeks. She was then seized with a serious purpura, having multiple hemorrhages from the nose and gums accompanied by hematuria. These symptoms continued for three weeks until she was in an extremely anemic condition, and there were grave fears for her life. The hemorrhages, however, ceased and her general condition improved rapidly.

<sup>1</sup> Presse Méd., 1906, xiv, 469.

<sup>2</sup> Bull. Soc. des Hôp., 1906, xxiii, 375.

Although numerous examinations of the chest were made it was not until fifteen days after the disappearance of the purpura that any evident signs of pulmonary tuberculosis could be found. Tubercle bacilli were found in the sputum and urine. The tuberculosis, without any other signs of purpura, advanced rapidly to cavity formation in six weeks.

There are numerous cases of purpura developing in individuals suffering with extrapulmonary tuberculosis. Gossner<sup>3</sup> reported a case of a man with a tuberculous testicle who had three repeated attacks of purpura before castration was performed, after which he had no further attacks of purpura. Coley and Ewing<sup>4</sup> have reported a fatal case of purpura hæmorrhagica occurring in the course of an acute lymphatic tuberculosis. There are also other instances reported in literature of purpura complicating chronic pleurisy, peritonitis, tuberculous adenitis, tuberculous cerebro-spinal meningitis, etc.

Bensaude and Rivet think that purpura is not infrequently associated with tuberculosis. Of their 35 cases of chronic purpura hæmorrhagica, 7 occurred in individuals undoubtedly tuberculous and 5 in individuals probably tuberculous. They say that in the presence of a purpura, particularly in the recurring or chronic form, when the cause is not apparent, the clinician should, by all means in his power, look for some chronic tuberculous lesion either of the lungs, or of the glands or of some other portion of the body. Brown says that purpura hæmorrhagica rarely occurs in tuberculosis. In the last 1000 cases at the Adirondack Cottage Sanitarium but 3 cases have occurred. This corresponds very closely to my figures. Out of 1626 ward patients at the Phipps Institute, I was able to find only 8 cases of purpura. Mackenzie, in 200 cases of purpura, found it associated with tuberculosis 4 times. Pratt,<sup>5</sup> in 258 cases of purpura, both primary and secondary, found it associated with tuberculosis 7 times.

The pathogenesis of purpura is still an undecided question. Weichell thought that the purpura was caused by the absorption of toxins from a rapidly breaking-down tuberculous area. Some of the writers have been inclined to lay the cause to a secondary infection, such as the case reported by Widal and Thérèse in which the blood and different organs contained streptococci. This finding, according to the different investigators has been rare. Others have favored the tubercle bacillus as the direct cause, since it has been clearly demonstrated by Jousset,<sup>6</sup> Rosenberger,<sup>7</sup> and others that the tubercle bacillus can be found in the circulating blood of both acute and chronic tuberculosis. Grenet,<sup>8</sup> in his experi-

<sup>3</sup> Münch. med. Woch., 1902, p. 451.

<sup>4</sup> Trans. Assoc. Amer. Phys., 1911, xxvi, 178.

<sup>5</sup> Osler's Modern Medicine, vol. iv, p. 681.

<sup>6</sup> Semaine Méd., 1903, p. 153; 1904, p. 289.

<sup>7</sup> AMER. JOUR. MED. SCI., 1909, p. 267.

<sup>8</sup> Comptes Rendu de la Soc. de Biol., 1903, p. 1509; *ibid.*, p. 1568; Thèse, Paris, 1905.

mental studies on purpura, found that three factors were necessary for its production: (1) An hepatic lesion; (2) nervous injury, and (3) an intoxication which acted locally on the nervous system. He says that in purpura there is a toxin that acts as a vasodilator by means of the nervous system, and that if the blood is altered by a lesion of the liver or some other viscera then cutaneous hemorrhage results from the localized vasodilatation.

There have been two fairly constant changes found in the blood of purpura hæmorrhagica: The diminution in the number of blood platelets and the failure of the blood clot to contract and express the serum. Bensaude and Rivet<sup>9</sup> classify their cases of purpura according to the blood pictures into two groups. The first includes the simple, rheumatic, toxic, and nervous purpuras and is characterized by a contraction of the clot, with no diminution in the number of the blood platelets. The diminution of the blood platelets and the absence of the contractility of the clot are the characteristics of the second group, and in this group are placed all the forms of purpura with large subcutaneous hemorrhages and hemorrhages from the mucous membrane and viscera.

The occurrence of purpura, especially the hemorrhagic form, in the course of a tuberculosis is always a grave symptom. It either marks the terminal or cachectic stage of the disease or an acute exacerbation of the tuberculosis which may go on to a rapidly fatal termination or from which the patient may recover. But always after the attack of purpura the examination will reveal a more advanced condition of the lesion.

All my 8 cases occurred in the terminal stage of chronic pulmonary tuberculosis. Case I, was an undoubted case of purpura hæmorrhagica, and occurred only five days before death. Case II, although there was hematuria, and at one time bloody stools accompanying a diarrhea, was, I believe, a simple purpura; the hematuria being accounted for by the tuberculosis of the kidney, ureter, and bladder. Cases III, IV, V, and VI were undoubtedly instances of simple or cachectic purpura. The last 3 were not discovered during life. Case VII, where the thrombosis of the internal saphenous vein was the exciting cause, was what Osler calls a mechanical purpura, being caused by a venous stasis. My last case, Case VIII, might be called either a simple purpura complicating the tuberculosis or a toxic purpura complicating the intense jaundice. Whether, however, a simple or a toxic purpura it was a purpura occurring at the termination of chronic pulmonary tuberculosis complicated by a most unusual form of caseous tuberculosis of the liver.

CASE I, No. 2657.—An Italian boy, aged sixteen years, was admitted to the wards of the Phipps Institute, August 5, 1904.

<sup>9</sup> Loc. cit.

His father died at the age of thirty-three years of some unknown cause and his mother at the age of twenty-seven due to some accident incident to childbirth. He had an attack of influenza in February, 1904, otherwise had had no previous illness. He gave a history of having lost about 30 pounds in the last year and a half. He had had a hemorrhage from the lungs in December, 1903. Since April, 1904, he complained of cough, which was most troublesome at night, accompanied by a moderate amount of yellowish sputum. He had pain in the anterior aspect of his right chest, dyspnea on exertion, had had several attacks of hoarseness, poor appetite, vomited occasionally, and also had diarrhea. Formerly he had had night sweats and some edema of feet. The examination showed an emaciated boy, with no enlargement of the cervical, axillary, or inguinal glands, and no signs of curved nails or clubbed fingers. The heart showed nothing abnormal. The examination of the right lung showed a large cavity in the upper lobe, with more or less disease of the remainder of that lung. The left lung showed a possible cavity at the apex and some disseminated tubercles throughout the lung. There was in addition peritoneal tuberculosis. The boy was extremely ill, but had been doing well until September 15, about six weeks after his admission. At that time there occurred several small hemorrhages from the bowel, followed in a few hours by a marked hemorrhagic eruption over the abdomen. He complained of no pain. On the morning of the seventeenth his nose began to bleed and the hemorrhagic eruption appeared on the chest. In spite of plugging the nostrils the nose continued to bleed slowly, but persistently, all of the seventeenth and part of the eighteenth, and on the nineteenth there was still a tendency to bleed. The eruption on the nineteenth was most marked over the abdomen, it was fading in places but these were interspersed with fresher areas. Over the anterior chest there were scattered spots, as well as on both arms and on the back of the left wrist. On the back there were two or three small spots. There was no eruption over the pelvis or lower extremities. The patient died early in the day of September 20.

The autopsy performed later on that day showed an ulcerative and miliary tuberculosis of both lungs, pleural adhesions, parenchymatous nephritis, fatty liver, tuberculous enteritis, enterorrhagia, petechiæ in skin and in the pleura and pericardium, and enlarged mesenteric glands.

CASE II, No. 2494.—A white man, aged twenty-three years, was admitted to the wards of the Phipps Institute June 10, 1904. His father had died at the age of fifty-five of heart disease. His mother, four brothers, and three sisters were living and well. Five brothers were dead, one having died of some disease of the bone and one of tetanus, the other three of unknown causes. One sister died in infancy. Three years before he had had an attack

of influenza and six months previously he had typhoid fever, followed in two months by rheumatism. In the last nine months he had lost twenty-two pounds, and complained of pain in both sides of chest in damp weather, cough, worse in the mornings, accompanied by considerable greenish sputum, marked dyspnea on exertion, occasional attacks of vomiting, diarrhea, night sweats, and slight edema of the feet. Examination showed an emaciated man. His heart was enlarged to the right and left. There was accentuation of both second sounds at the base. No murmurs were recorded. There was advanced disease of both lungs with cavities at both apices. His progress was fairly satisfactory for the first month, then he began complaining of painful urination with the passage of some gravel. His condition continued gradually to grow worse during August, his abdomen became distended and tympanitic, and he still complained of pain on urination, passing gravel and now also some blood. During September these symptoms continued, and on October 20, he developed a severe diarrhea, almost dysenteric in character, the stools containing much blood and mucus. By October 24, the diarrhea was greatly improved and there was no blood in the stools, but the patient was weak and losing ground rapidly. The diarrhea returned in a few days, but was not so severe as at first. On October 31, there appeared a purpuric rash all over the abdomen and extending up over the sternum to the level of the fourth rib. The patient died the next day.

The autopsy, performed the same day as the death, showed ulcerative and miliary tuberculosis of both lungs, pleurisy, tuberculosis of intestines, appendix, left kidney, ureter, and bladder, and cloudy swelling of right kidney, and enlarged mesenteric and bronchial glands.

CASE III, No. 5473.—A woman, aged fifty-seven years, was admitted to the wards of the Phipps Institute, September 13, 1907. Her father had died at sixty-three of paralysis, and her mother at fifty-four of consumption. She had one brother living and well, three sisters living, two in good health, and one suffering with tuberculosis. Five brothers had died, one of consumption. She had had pleurisy and influenza two years before and rheumatism one year previously. She had not been well since her pleurisy, having lost over 60 pounds, and complaining of cough, worse at night, and in the early morning, accompanied by considerable yellowish expectoration. She had dyspnea on exertion, poor appetite, some slight soreness in epigastrium after eating, two loose stools a day, and slight edema of the ankles. A month previous to admission she had had night sweats. Menopause had taken place ten years before. Examination on admission showed an emaciated woman, with cheeks injected and slightly flushed, sordes on lips, and slightly curved nails. The heart was normal.



The examination of the lungs revealed an infiltration of the right upper lobe, a large cavity in the left upper lobe, a cavity in the upper part of the lower left lobe, with scattered infiltration below. The abdominal examination was negative. The course of the case was progressive, and in the beginning of October she developed a severe diarrhea. On October 10, about one month after admission, she showed on her forearms and legs a few small discrete, dark petechiæ, more marked toward the extremities. She died on October 21.

The autopsy showed chronic fibroid pleurisy of both sides, chronic empyema on the left side, chronic pulmonary tuberculosis of lungs with cavity formation, collapse of left lung from the empyema, emphysema (compensatory) of the right lung, interstitial myocarditis, atheroma of the aorta, cirrhosis of the liver with fatty infiltration, tubercles of liver, spleen and tonsils, ptosis of the intestines, chronic enteritis with tuberculous ulceration, chronic obliterative appendicitis, diffuse nephritis, and congestion of the spleen, tonsils, and mesenteric glands.

CASE IV, No. 2815.—A white woman, aged twenty-eight years, was admitted to the wards of the Phipps Institute on October 18, 1904. Her father died when aged forty years, of some unknown cause. Mother and one sister had died of phthisis. One brother and one sister were living and well. She had had pneumonia as a baby and malaria four years before admission. She gave a history of about 2 pounds loss in weight, cough with a small amount of greenish-yellow expectoration for nine months, some pain in shoulder blades, dyspnea on exertion, poor appetite, vomiting three weeks before, loose bowels, night sweats two months previously, slight edema of the feet, and the menses suppressed for four months. Examination showed an emaciated woman, with heart and abdomen normal, and advanced disease of the right lung, with cavities in the upper half and an infiltration of the apex of the left lung. The patient ran a rapid acute course and died on November 9, 1904.

The autopsy performed the next day showed ulcerative tuberculosis of both lungs with pleurisy, red atrophy of the liver, dilatation of the right heart, enlarged mesenteric and bronchial glands. There were noted on the inner aspect of the left thigh a few ecchymotic spots.

CASE V, No. 2664.—A white man, aged twenty-two years, was admitted to the wards of the Phipps Institute on August 8, 1904. His father, mother, two brothers, and two sisters were all living and well. He had had "typhoid-malaria" six years before and two attacks of pleuropneumonia, the first one two and a half years ago and the second one and a half years ago. Since his first attack of pleuropneumonia he had never been well, having lost about 45 pounds, and being troubled with a most distressing cough,

worse in the morning, and accompanied by considerable yellow expectoration. He had dyspnea on exertion, a fairly good appetite, three or four attacks a week of vomiting due to coughing, and regular bowel movements, recently a little streaked with blood. Examination on admission showed an anemic man not markedly emaciated. The abdomen was normal, and the heart showed mitral stenosis. The examination of the lungs revealed in the right upper lobe infiltration of the upper half, with miliary tubercles below, in the middle lobe miliary tubercles, in the lower lobe a close aggregation of miliary tubercles in the upper half and a few below, in the left upper lobe infiltration of the upper half and a close aggregation of miliary tubercles in rest of lobe, in lower left lobe a close aggregation of miliary tubercles in upper half and a few scattered below. The patient was in the hospital for six months, and was a sick man all the time, suffering greatly with dyspnea, distressing cough, and vomiting due to coughing. At the end of December and the first part of January he had several hemorrhages, one quite large, discharging over 10 ounces of blood. He continued spitting blood and suffering from his cough and dyspnea until he died on January 23.

The autopsy performed on January 24, showed a chronic tuberculosis of the lungs, with bronchopneumonia, chronic fibroid pleurisy of both sides, and parenchymatous nephritis. There were noted at autopsy a few red spots on the anterior surface of the abdomen.

CASE VI, No. 3451.—A white woman, aged twenty years, was admitted to the wards of the Phipps Institute on July 8, 1905. Her father died from drinking wood alcohol, and one brother died of hydrocephalus. Mother and two sisters are living and well. She had had influenza four years before. She gave a history that in the last eight months she had lost about 40 pounds, and had had for the last six months cough, worse at night, and accompanied by considerable yellowish-green expectoration, dyspnea on exertion, slight hoarseness at times, night sweats, variable appetite, vomiting at times, regular bowel movements, and suppressed menses for the last three months. Examination showed a fairly well-nourished woman. Her heart was normal, right kidney freely movable, otherwise the abdomen was normal. Lungs showed fairly advanced disease with a cavity in the right upper lobe. Her disease ran an acute course, and the patient died on November 13.

The autopsy performed the following day showed chronic fibroid pleurisy of the right side, chronic tuberculosis of the lungs, with cavity formation and edema, dilatation of the heart, atheroma of the aorta, fatty changes of the liver with congestion, and miliary tubercles, gastroptosis, tuberculous enteritis, diffuse nephritis, tuberculous adenitis, and tuberculous tonsillitis with amyloid

changes. It was noted that the face, back of the hands, chest, and shoulders showed a reddish-yellow discoloration. The inner surface of each leg had a few reddish-yellow blotches.

CASE VII, No. 2768.—A white man, aged thirty-three years, was admitted to the wards of the Phipps Institute October 3, 1904. His father died at the age of sixty-four years of typhoid fever. His mother, one brother, and five sisters were living and well. He had never been sick. He gave a history of cough and expectoration for two years. Three months before admission he had a hemorrhage from the lungs and his cough became more severe, with moderate amount of greenish expectoration. He suffered with dyspnea on exertion, slight hoarseness for a long time, frequent night sweats, and poor appetite, but no gastric symptoms. He had lost 50 pounds in the last three months. Examination on admission showed an emaciated man with a very hectic countenance. His heart was normal. Lungs showed advanced disease. There were cavities in the right upper and middle lobes and in the upper part of the lower lobe with miliary tubercles below. The left lung showed a small cavity at the apex with emphysema and miliary tubercles throughout the rest of the lung. Patient was extremely sick and very weak. He had an active miliary condition apparently following his hemorrhage three months previously. During the night previous to November 7 he was seized with a severe pain in the left leg. On the morning of November 7, the whole leg and thigh were slightly swollen with some pitting. There was cyanosis of the limb with numerous small purple spots which did not disappear on pressure. No special area of tenderness was found. In the afternoon of November 7, the pain was much less, and there was extreme tenderness on pressure on the veins in the popliteal area and for 3 inches upward. On November 9, his condition was much the same. He had had no return of pain and the tenderness was less. The purpuric spots were fading out a little. By November 14, the leg was no longer tender, but still retained some of the edema. He continued to grow weaker, and on November 23, died.

The autopsy performed the same day, showed a pneumothorax on the right side, effusion on the right side, caseous pneumonia of both lungs, with ulcerative tuberculosis of right lung, edema, and congestion of both lungs, fatty kidneys, displacement of liver, fatty infiltration of liver, pleurisy, enlarged bronchial glands, and thrombosis of the left internal saphenous vein.

CASE VIII, No. 2662.—A white woman, aged forty years, was admitted to the wards of the Phipps Institute August 8, 1904. Her father died at the age of forty-five years of tuberculosis. Mother died at the age of thirty years in confinement. She had one brother and one sister living and well. Two sisters died very young of some unknown cause. She had never been sick, but gave a history of excessive use of alcohol over a long period of time.

In the last two years she had lost 60 pounds, and for the last six months had had a cough, worse at night, accompanied by a profuse yellow expectoration. She complained of pain in lower anterior part of her right chest, dyspnea on exertion, attacks of hoarseness lasting several days at a time, poor appetite, epigastric pain, distress after eating, constipation, passing blood in the stools, night sweats, and slight edema of the ankles. Examination on admission showed an emaciated body, with a face of fairly good color. The heart was normal as well as the abdomen. The lungs showed infiltration of the upper part of the right upper lobe, consolidation with some softening of the left upper lobe. (This is a note made on the day of the examination that the prostration and loss of weight is out of all proportion to the pulmonary involvement.) On August 25, the liver was found slightly enlarged, edge very hard, but smooth and not tender. On September 21, the patient was markedly jaundiced; liver slightly enlarged. Pressure in the epigastrium caused a great deal of pain. No mass could be felt. On September 26, blood examination showed the erythrocytes, 3,840,000; leukocytes, 10,000. The blood was pale and coagulated slowly. The jaundice had become more marked. The conjunctivæ were of a bright yellow color. The whole body was now deeply jaundiced and pain in the epigastric region was more marked. Liver was distinctly palpable, and the edge was sharp and hard. The enlargement was more apparent in the left lobe. On October 1, the jaundice was intense, the abdomen flabby, and distended. There was some free fluid in the peritoneal cavity. Several purpuric spots appeared on the abdomen. From this time on the patient rapidly grew weaker, the jaundice being extreme, pain marked in the epigastrium, sordes on teeth and tongue, pulse weak and irregular, and she finally died on October 7.

The autopsy on October 8, showed ulcerated tuberculosis of the left lung, tuberculous pneumonia and edema of the right lung, miliary tuberculosis of the spleen, fatty infiltration of the heart, fatty kidneys, with tubercles, and an unusual caseous tuberculosis of the liver with cirrhosis.

#### ADDITIONAL REFERENCES.

- Bauer. *Münch. med. Woch.*, 1902, p. 748.  
 Cohn. *Ibid.*, 1901, p. 2001.  
 Dumas. *Arch. de méd. mil.*, 1903, xlv, 527.  
 Lion and Le Blage. *Bull. Soc. des Hôp.*, 1910, xxviii, 481.  
 Mackenzie. *Allbutt's System of Medicine*, vol. v, p. 572.  
 Moizard and Grenet. *Gaz. des Hôp.*, 1903, lxxvi, 1437.  
 Osler. *Practice of Medicine*, p. 742.  
 Pratt, Eldon. *Brit. Med. Jour.*, 1901, xi, 865.  
 Robert. *Thèse*, Paris, 1904.  
 Raemisch. *Münch. med. Woch.*, 1902, p. 66.

## REVIEWS

---

A TREATISE ON DISEASES OF THE HAIR. By GEORGE THOMAS JACKSON, M.D., Professor of Dermatology in the College of Physicians and Surgeons, Medical Department of Columbia University, and CHARLES WOOD McMURTRY, M.D., Instructor in Dermatology in the College of Physicians and Surgeons, Medical Department of Columbia University, New York. Pp. 366; 109 engravings and 10 colored plates. Philadelphia and New York: Lea & Febiger, 1912.

IN this treatise the authors have endeavored to present "all that is known about diseases of the hair and scalp;" and they have performed their task with a thoroughness and wealth of detail that has left no aspect of the subject unconsidered. It is divided into five sections: Anatomy, Physiology, and Hygiene of the Hair; Essential Diseases of the Hair; Inflammatory Diseases of the Hair Follicles; Parasitic Diseases of the Hair; and Diseases of the Hair Secondary to Diseases of the Skin.

The excellent chapter on the care of the hair and scalp concludes with a short section on barber shops and hair-dressing establishments which are regarded as "The most fertile single source of spreading diseases of the hair and scalp;" and some much needed advice is given concerning the proper management of such establishments, advice which if followed would go far to eliminate the danger of transmitting disease.

Among other important essential diseases of the hair the various forms of alopecia are considered at length. The authors regard some form of seborrhea as the exciting cause of one of the commonest forms of premature loss of hair, alopecia pityrodés; and they put themselves squarely on the side of the contagionists, declaring that "As seborrheal dermatitis and pityriasis steatoides are contagious diseases, and very prevalent, the wonder is not that so many people lose their hair, but that more do not." The parasitic origin of alopecia areata, however, which has many supporters, especially among the French, is not regarded as proved although it is not to be altogether rejected. Among the many medicinal agents recommended for stimulating the growth of hair in the several varieties of baldness pilocarpin is believed to be of decided value while crude petroleum which has long had a con-

siderable reputation, particularly among the laity, as a hair grower has been found useless.

The parasitic diseases of the scalp and beard are treated at great length, 65 pages being devoted to the subject of ringworm alone, a subject which is treated in a manner fully justifying the authors' statement made in the preface that "In no other book, excepting those of Sabouraud, will be found so complete a presentation of what is known about ringworm." Of the forty species of fungi concerned in the production of this very common malady enumerated by Sabouraud, twelve of the commonest are described together with the clinical symptoms and cultural features peculiar to each. In the treatment of this usually obstinate and troublesome affection preference is given to the x-ray when this is available, employing the technique of Sabouraud.

But one form of seborrhea is recognized, seborrhea oleosa, the seborrhea sicca of the text-books being in the opinion of the authors, not a seborrhea at all. This latter affection is described as pityriasis of which there are two forms, pityriasis simplex and pityriasis steatoides, the latter form being identical with eczema seborrhoicum. The bacterial origin of seborrhea is regarded as probable but not yet proved, but pityriasis simplex is believed to be caused by the organism first described by Malassez identical with the *flaschenbacillus* of Unna.

The majority of the diseases discussed in the final section of the treatise, including such affections as, acne necrotica, psoriasis, lupus erythematosus, scleroderma, etc., are, of course, not diseases of the hair at all, but are included because they frequently occur upon the scalp or other hairy regions.

The volume is well illustrated, containing more than a hundred engravings and ten colored plates, most of them of unusual excellence, which add much to its value.

In conclusion, this treatise which is remarkably complete and up to date, is easily the best work upon diseases of the hair which has yet appeared.

M. B. H.

---

PHARMACOLOGY AND THERAPEUTICS. By H. C. WOOD, JR., M.D., Professor of Pharmacology and Therapeutics in the Medico-Chirurgical College of Philadelphia. Pp. 429; 26 illustrations. Philadelphia: J. B. Lippincott Co., 1912.

IN his text-book on Pharmacology and Therapeutics, Dr. Wood writes clearly and concisely and with not more than the necessary dogmatism. He has eliminated non-essentials and confusing discussions of facts which are of doubtful interpretation. His grouping of drugs is based on what he considers their most important therapeutic application, and as therapeutics is emphasized as strongly as pharmacology, such an arrangement is a logical one.

At the conclusion of the account of each drug, a short bibliography is inserted covering the more important publications concerning them. Some slight criticism may be offered of this feature of the book. The list of references is, at times, too curtailed. For example, under digitalis, none of the numerous and important contributions of Hatcher is mentioned. Again it would seem desirable to indicate what particular reference has to do with certain facts given in the text, since otherwise it might become necessary to look through the entire list before the original authority for a statement is found.

With regard to other features of the book, it is unfortunate that at a time when teachers of prescription writing are urging the use of the metric system, and when this system is given preference in the pharmacopœia, Dr. Wood should place more emphasis on the system of apothecaries' weights and measures. In his chapter on prescription writing, he uses the latter entirely in his prescription examples, and again in the dosage given for each drug, this system is given first place.

Concerning the matter in the text in general, the chief criticism is that too much brevity has been exercised. For example, no mention is made of antitoxins and vaccines, which have now a very definite place in therapeutics. In the chapter on bromides, no mention is made of the inter-relationship of bromides and chlorides, a matter of considerable pharmacological interest and therapeutic importance. In the introductory chapter on the mode of administration of drugs, the technical aspects of the subject should be described at greater length. It would be quite proper, for example, to give a full description of the method of intravenous injection. This would be directly applicable to the administration of salvarsan in syphilis, and an authoritative statement of the technique of neutralization and injection of this drug would be of value to readers of the book. The author's apparent preference for giving mercury by the stomach in the treatment of syphilis will undoubtedly not be approved by the majority of syphilographers, who believe so thoroughly in intramuscular injection.

Under the digitalis group, the therapeutic uses are prescribed in far too condensed a form. This subject has been studied extensively by Cushny and others, and the conclusions arrived at are of the greatest importance to the practitioner. Cushny has also called attention to the infrequent occurrence of the so-called cumulative action of digitalis, and has emphasized the fact that vomiting is the first and usually the only symptom of overdosage during continued medication. The work recently done along these lines should by all means be incorporated in the text.

On the whole, Dr. Wood's book shows great industry and familiarity with recent literature, and omissions such as have been noted are perhaps to be expected in a first edition. G. B. W.

**SURGICAL AFTER-TREATMENT.** By L. R. G. CRANDON, M.D., Assistant in Surgery at Harvard Medical School, and ALBERT EHRENFRIED, M.D., Assistant in Anatomy at Harvard Medical School. Second edition. Pp. 831; 264 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

THE success which this work has had causing a revision and second edition in so short a space of time, is commentary enough upon its need and value.

As its name implies, this is simply an after-treatment to surgical procedures and as such should prove of the greatest value not to surgeons alone, but to those also who not being surgeons are left in charge of cases when the services of the surgeon are no longer available. This is especially true if the case has been left under the care of a practitioner who has not had any recent surgical experience.

The authors have divided the book into two parts. In the first there are thirty-nine chapters devoted to the care of the patient and the alleviation of various symptoms. Here many practical points are brought up which the young house surgeon is only too apt to leave to the nurse and which the busy practitioner out of touch with modern hospital methods is often at a loss to know how to handle.

The subject of the treatment of the patient after the administration of an anesthetic and the various methods for relieving the nausea and vomiting and the accompanying thirst are carefully taken up. The manner of giving enteroclysis is correctly shown, and similar treatments are likewise elucidated, all of which are rational and good. In addition, the illustrations which accompany the descriptions are excellent and are of the greatest practical assistance in making the text clear.

Not only to the physician will these chapters in the first part of the book be of use, but to the nurse as well, especially should she happen to be one who has had only a limited training in the care of the sick.

The discussion of bandaging, though brief, is to the point, and covers most of the important facts upon that subject which are essential in such a work.

There are certain chapters in this section such as Foreign Bodies Left in the Abdominal Cavity, Adhesions, and Preparation of the Patient for Operation, which hardly come within the scope of a book upon surgical after-treatment, and which could well be omitted and the book improved by thus having its bulk diminished.

In the second part the remaining fourteen chapters of the book with the exception of the last two, are devoted to various operations and their after-treatment. In these chapters the authors are clear and concise and do not confuse the reader by too many



methods, usually limiting themselves to one good method of treatment. Here, too, the illustrations are numerous and well chosen and greatly add to the text.

Very carefully and completely are the various parts of the body, with the operations peculiar to each, taken up and systematically discussed.

The last chapter but one is devoted to Therapeutic Immunization and Vaccine Therapy and has been most ably presented by Dr. George P. Sanborn, but is somewhat out of place in a work designed primarily for the practitioner rather than the specialist.

Throughout the whole work the authors have maintained an unusually high standard, and such a book cannot help but be of the greatest assistance to anyone who wishes to keep up with modern methods of surgical after-treatment.

F. P., JR.

---

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Volume I, No. 4. Pp. 154; 22 illustrations. Philadelphia and London: W. B. Saunders Company, August, 1912.

AMONG the most important of the many subjects discussed in the August number of Murphy's clinics are ankylosis of the knee, arthroplasty, and joint infection; hypertrophy of the prostate; old fracture of the elbow-joint; traumatic epilepsy, with decompression; carcinoma of the lip; and finally, a Student's Clinic, at the Northwestern University Medical School, devoted to a quiz on the subject of fractures, and to a discussion of joint infections.

There is no denying the interest which attaches to this series of publications. Though second thought and careful revision would, no doubt, make even Dr. Murphy desire to modify some of his statements and expunge others, it is not likely that any one of experience will take this magazine for other than it is—a stenographic report of clinics. It has neither the accuracy nor the system of a monograph, and if one wanted either to learn cold facts of science or to study details of operative procedure he certainly would not look in a publication which professedly comes red-hot from the printing press, and which even to casual inspection reveals such lack of editing as in a daily newspaper might be condoned, but which could not be overlooked in a monthly or quarterly periodical claiming for itself a certain literary prestige. Yet there are monographs and text-books in abundance, but only one "Murphy's Clinics;" and with all its faults we love it still.

A. P. C. A.

THE PRACTICE OF MEDICINE. A MANUAL FOR STUDENTS AND PRACTITIONERS. By HUGHES DAYTON, M.D., formerly of the Cornell University Medical School, New York. Second edition. Pp. 326. Philadelphia and New York: Lea & Febiger, 1912.

DAYTON, in this epitome of internal medicine, presents to the hurried practitioner and the undergraduate student, a brief treatise on the essentials of diagnosis and treatment. The classification of the various diseases, as well as the general form of presenting them, follows closely that used in Osler's practice. The salient features of the etiology, pathology, symptomatology, differential diagnosis, prognosis, and treatment of most diseases are described in a concise, brief, but thorough manner. The less important diseases are also carefully elucidated, but on account of the character of the book, the same attention cannot be directed to them as to the more frequent and hence, more important diseases.

The criticism of this book is such as applies to all books of this character. Disease presents so many variations and aspects that a brief description of a typical case can at the best be only suggestive. Hence, to elaborate the suggestions that have been conveyed to the reader recourse must be had eventually to the larger and more complete text-books.

There is no criticism to be made of the subject matter, which briefly includes the more recent advances in medicine, nor of the general appearance of the book, which is neat, well printed, and free from typographical errors.

J. H. M., JR.

---

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor of Therapeutics in the Jefferson Medical College, Philadelphia. Vol. III, September, 1912, pp. 353; 28 illustrations. Philadelphia and New York: Lea & Febiger.

As each successive number of *Progressive Medicine* comes to our attention we become increasingly impressed with the unquestioned merit and excellence of the contributions and the value of this publication to every practitioner who would keep abreast of the time.

Volume III for this year opens with a article of 86 pages by William Ewart on diseases of the thorax and its viscera. He begins by taking up tuberculosis and its treatment; he next dis-

cusses recent advances in percussion and auscultation of the chest; this is followed by a consideration of pulmonary edema, emphysema, pulmonary surgery, mountain sickness, compressed air illness, common colds, asthma, and an exhaustive review of the subject of atmotherapeutics. Under the heart and great vessels he discusses the various newer instruments of precision, certain physical signs that have recently attained importance, some interesting cardiac affections including paroxysmal tachycardia and "cardiac asthma," and heart treatment. He concludes with several pages devoted to a number of affections of other mediastinal organs.

William S. Gottheil calls attention to recent advances in dermatology and syphilis in a contribution of 40 pages. Among many interesting subjects considered are: Blue atrophy of the skin from cocaine injections, the early diagnosis of cancer of the skin, chancroid vaccine, the rational treatment of furunculosis, pruritus ani, and lichen planus in the negro. The last quarter of his article deals entirely with syphilis.

The contribution on obstetrics is furnished by Edward P. Davis, who devotes 150 pages to this important subject. He first takes up the diagnosis of pregnancy; then the urine in pregnancy; various phases of the toxemia of pregnancy; gestation complicated by tuberculosis and various other conditions; as well as many other important phases of the subject, notably eclampsia and placenta prævia. Under labor he discusses among other things labor during adolescence; complications of labor; and the treatment of labor complicated by operation for antefixation. The uterine muscle, abortion, and pituitrin are also considered and his excellent *resume* of the subject concludes with interesting sections on obstetric surgery, the puerperal period, and affections of the newborn.

The final chapter of the volume is by William G. Spiller, from whom we have learned to expect without fear of disappointment an able discussion of diseases of the nervous system. His present review of the subject embraces 52 pages and is fully up to the high standard he has set in all his previous contributions. G. M. P.

---

THE PITUITARY BODY AND ITS DISORDERS. CLINICAL STATES PRODUCED BY DISORDERS OF THE HYPOPHYSIS CEREBRI. By HARVEY CUSHING, M.D., Associate Professor of Surgery in the Johns Hopkins University, Professor of Surgery (elect) Harvard University. An amplification of the Harvey Lecture for December, 1910. Pp. 341, with 319 illustrations. Philadelphia: J. B. Lippincott Company, 1912.

DR. CUSHING with his usual originality has succeeded in arousing the attention of the medical profession. He has collected an

enormous amount of material regarding the pituitary body much of which is original and the result of careful clinical observation and experiment. Not all the statements that he makes in all probability will be confirmed by further study, but of this fact he is keenly aware. His book is that most valuable of all forms of medical publications, a painstaking monograph, and should appeal to many classes of the medical profession, to the physiologist, to the surgeon, and above all to the clinician.

The four main types of pituitary disease are gigantism and acromegaly produced respectively it is supposed by overaction of the pituitary gland in youth and in adult life; infantism and adiposity produced by the deficient action of the gland before and after puberty. Combinations occur and we are not yet able to differentiate with precision all the functions of the different parts of the gland, but at least the material available for our knowledge has been presented in a clear and logical manner.

The number of illustrations is remarkable, but they are all illustrative and there is actually no padding, a fault that few medical books escape. Perhaps the most useful original communication is the attempt to devise a method of administering pituitary extract in a rational and adequate manner to cases needing it. A few typographical errors have crept in, but they do not apparently in any instance mar the clearness of the text. The taste of the reviewer is against the splitting of the infinitive but Dr. Cushing appears to prefer it. It has at least the authority of frequent usage at the present day.

The work is a distinct contribution to medical literature, perhaps one of the most notable of the year.

J. S.

---

DISEASES OF THE STOMACH WITH ESPECIAL REFERENCE TO TREATMENT. By CHARLES D. AARON, Sc.D., M.D., Professor of Gastro-enterology and Adjunct Professor of Dietetics in the Detroit College of Medicine; Professor of Diseases of the Stomach and Intestines in the Detroit Post-graduate School of Medicine, Consulting Gastro-enterologist to Harper Hospital. Pp. 555, with 42 illustrations and 21 plates. Philadelphia and New York: Lea & Febiger.

DR. AARON has contrived to write a work upon diseases of the stomach and to avoid more or less completely the conventional lines of the text-book. The material that he has included is somewhat unusual and it almost seems as if he had kept a notebook in which he recorded various things that might be useful in his practice and had later incorporated the best of these in his book.

It is obvious that it is not possible in a work of this kind to be wholly original, but Dr. Aaron manages frequently to present old facts in a refreshing manner.

The first part of the book is devoted to physiology and methods. A somewhat ambitious effort is made to reproduce the color reactions, but as these can be learned so readily in the laboratory with artificial solutions and as the reproductions of the colors are never absolutely exact, the result is not always satisfactory. In the chapter on diet tables are introduced of the various types of diet, the European origin of which has not been as completely disguised as one would like in an American text-book. Then follows several chapters on methods of treatment, that on hydrotherapy being particularly useful, and a very valuable chapter upon surgical intervention.

Dr. Aaron has not successfully resisted the temptation to devise an abdominal bandage and corset, but if this is a fault it is so commonly perpetrated by those engaged in the study of diseases of the gastro-intestinal tract that he should receive ready absolution. The functional diseases of the stomach, particularly motor insufficiency are well discussed and there is a valuable chapter upon gastric hemorrhage.

Altogether the book can be commended as one of the best of the recent works published on the subject. J. S.

#### PRIMARY MALIGNANT GROWTHS OF THE LUNGS AND BRONCHI.

By I. ADLER, A.M., M.D., Professor Emeritus at the New York Polyclinic. Pp. 325; 16 plates and a colored frontispiece. New York, London, Bombay, and Calcutta: Longmans, Green & Co., 1912.

THIS very scholarly monograph, which represents a vast amount of labor in its compilation, will fill an important place among reference handbooks concerning a condition little known and seldom considered in the differential diagnosis of diseases of the chest. It will serve also to focus more attention on the possibility of malignancy in doubtful cases. The author desires to bring home the fact that primary tumors of the lungs are not so exceedingly rare as is commonly supposed, and remarks justly enough that for the majority, "the ubiquitous tuberculosis with its multi-form clinical appearances, and its plastic adaptations to all ages and all conditions of mankind, is ever ready to furnish to all but a very few, a comfortable and satisfactory diagnosis."

Of the 325 pages, 105 are devoted to a consideration of the etiological, pathological, and clinical features of pulmonary neo-

plasms (excluding primary growths of the pleura). The remaining 220 pages are taken up with analytical tables of all cases reported up to the time of publication, comprising 374 cases of carcinoma, 90 cases of sarcoma, 99 classified as doubtful, and 18 miscellaneous tumors. Tables are appended with figures concerning the duration of life in carcinoma and sarcoma cases and the location of metastases.

Adler states as the present consensus of opinion that primary carcinomas of the lung develop from the bronchi and are strictly bronchial carcinomas; that on the other hand, carcinoma starting from lung tissue does occur, but is very rare and is built up not of flat but of cylindrical epithelium. He discusses at some length the nature of endotheliomas, and shares the views of those who oppose the classification of tumors according to the three germinal layers. Another chapter deals in an interesting manner with the various conflicting views concerning metaplasia, not, however, with reference to pulmonary neoplasms in particular.

In the description of the clinical features associated with malignant growths in the lungs, the following symptoms appear most prominently. In the early stages, a rather insignificant but fairly constant cough, mostly without expectoration; the presence in the sputum of large spherical cells filled with a multitude of fatty granules; paralysis of the recurrent laryngeal nerve in the presence of malignant effusions; and a loss of weight and strength. As aids to diagnosis, he urges the routine use of the *x*-rays, and of the bronchoscope, which, he believes, is of use in detecting the growths occupying the upper bronchi. He urges in suspected cases, the practice of exploratory thoracotomy. The plates, chiefly representing histological preparations, are for the most part admirable.

H. G. S.

---

THE PRINCIPLES OF ANATOMY. THE ABDOMEN PROPER DESCRIBED AND ILLUSTRATED BY TEXT AND PLATES. By WM. CUTHBERT MORTON, M.A., M.D. (Edin.). Pp. 159; 28 illustrations. New York: Rebman Company.

ONLY the abdomen is considered in this the first portion of what is intended to be a work on the anatomy of the whole body. Morton presents a method of studying anatomy which differs considerably from that usually employed in medical schools. It is intended not to rival, but to stimulate practical study, and to unify the host of impressions gained at the dissecting table, in the lecture room, at the bedside, and in the operating room. It substitutes for the usual text-book, made up chiefly of text with more or less profuse illustrations; a small text-book in which there are a few illustrations, and a series of 28 large plates or 14 front-and-

back plates. The book, after discussing the underlying principles of the method and the plates, which are kept separately in a portfolio, gives directions for the dissection of the abdomen. Then follows the descriptive text, which is largely a brief outline of the various organs and other structures, and is apparently supplementary to the plates. These are artistic, but purely diagrammatic, and presumably as accurate as such illustrations can be. Each plate may be inspected separately, or by transillumination, when the whole of each organ can be seen in outline and the front and back plates correlated with each other. By combined inspection by means of cut-out leaves, one obtains a front view of certain organs lying at different depths and a similar back view of others.

A trying out of the method will be necessary to determine its value. The finding and tracing of the various structures on the plates, after the reading of the text, will tend to fix the facts more firmly in the student's mind, but it is possible that this will be at the expense of too much time, because of the necessary frequent passing from text to illustration, which is not aided by signs or numbers. Nor is it evident that the impression left in the student's mind is clearer and more lasting than that obtained by the usual method of study. The same time given to the accepted text-books, the various models, and cadaver preparations, dissections and sections, usually available to the present-day student, would probably give better results. A book on anatomy must be incomplete which does not include a consideration of microscopic anatomy, but this could hardly be expected in a work the chief object of which is to teach by illustrations.

T. T. T.

---

MY METHOD OF PREPARING THE OPERATIVE FIELD WITH TINCTURE OF IODINE. By KGL. RAT DR. ANTONIO GROSSICH, Chief Surgeon of the City Hospital in Fiume. Pp. 80. Berlin and Vienna: Urban & Schwarzenberg.

GROSSICH presents, in the form of a monograph, his conception of the position now occupied by his iodine method of preparing the skin of the operative field. That it has been a valuable contribution to operative surgery needs no discussion. In the four years since its introduction its recognition has become world-wide, and this full presentation of the whole subject will receive, undoubtedly, a cordial and wide reception. It is a general summing up of the work done by Grossich and others. He discusses his experience in 3759 surgical and gynecological cases, dividing them into those of accidental wounds, aseptic and septic operations, and emphasizes especially its value in the treatment of accidental

wounds. A separate section is devoted to the various objections raised against the method, such as the development of eczema, adhesions between coils of intestines from irritation due to contact with the iodine-covered abdominal skin during the operation, and conjunctivitis. The importance of avoiding all washing before applying the iodine is emphasized. Those who wish to become familiar with the method in all its details will find here all the necessary information, including a brief abstract of all papers published on the subject.

T. T. T.

---

AN INDEX OF TREATMENT BY VARIOUS WRITERS. Edited by ROBERT HUTCHISON, M.D., F.R.C.P., Physician to the London Hospital, etc., and H. STANSFIELD COLLIER, F.R.C.S., Surgeon to St. Mary's Hospital, Joint Lecturer on Surgery in St. Mary's Hospital Medical School, etc. Revised to conform with American usage. By WARREN COLEMAN, M.D., Professor of Clinical Medicine and Applied Pharmacology, Cornell University Medical School, etc. Sixth edition, revised and enlarged. Pp. 1051; 67 illustrations. New York: William Wood & Co., 1912.

THE demand for short-cut methods in the practice of medicine is much in evidence at the present time, as shown by the numerous digests of literature, compends, and in the present instance in the demand for a sixth edition of the work before us. The effect of these short-cut methods on general medical work may be questioned. There is already too much of a tendency among physicians to superficiality and symptomatic treatment without striking at the root or actual cause of the disorder, and we fear that these condensed and abbreviated compends rather foster than discourage this tendency.

In the present work the authors have attempted to provide the practitioner with a complete guide to treatment in moderate compass and in a form convenient for reference. They have been fortunate in securing the coöperation of a group of contributors of special experience whose names will be a sufficient guarantee of the value of the text, and no pains have been spared to make the book a trustworthy index to the best and most modern methods of dealing with disease. In the present edition all of the old articles have been thoroughly revised and many new ones included, among which are those on puerperal sepsis, hydro- photo- and thermotherapy, and treatment by carbonic snow, along with a good number of shorter ones.

The work is remarkably thorough for a work of its kind, and covers a multitude of subjects. The individual articles have the



signature of the contributor, adding considerably to their trustworthiness. The directions are clear and concise, and confine themselves usually to one line of treatment which has been tried and proved to be reliable. With a work of such broad scope there are bound to be minor omissions, and the present volume is not free from this error. The treatment in some instances falls into the fault of being too symptomatic and shotgun in type. The drugs and prescriptions, although made to conform in the main to American usage, nevertheless bear their English stamp. The printing while small is unusually clear and distinct, the paragraphs well-marked, and the entire work remarkably free of typographical errors. While we would hesitate to recommend the book as a single book to be depended on, it is certainly an addition to our books of handy reference so useful in the hustle of busy practice. It should, however, be used along with works on general diagnosis and pathology.

F. H. K.

---

THE SKIAGRAPHY OF THE ACCESSORY NASAL SINUSES. By A. LOGAN TURNER, M.D., F.R.C.S.E., F.R.S.E., Surgeon to the Ear and Throat Department, the Royal Infirmary, Edinburgh; Lecturer on Diseases of the Ear, Nose, and Throat, University of Edinburgh, and W. G. PORTER, M.B., B.Sc., F.R.C.S.E., Surgeon to the Eye, Ear, and Throat Infirmary, Edinburgh. Pp. 127, with 45 half-tone reproductions from radiographs and 3 drawings. Edinburgh and London: William Green & Sons, 1912.

THIS book seems to represent an effort on the part of the authors to demonstrate to their fellow specialists the assistance to be gained by radiography in the diagnosis of accessory sinus disease, and to aid in the difficult interpretation of the complicated radiographs of the head. With these ends in view, the authors have succeeded admirably in their purpose. The handling of the subject by rhinologists renders it better adapted, perhaps, to the comprehension of the followers of this specialty than would be the case if it were presented from the standpoint of the Röntgenologist. The former is made to realize just what dependence he can place upon radiography to aid him in diagnosis. The Röntgenologist who has had but a limited experience in sinus work will find much of value in this book to aid him in learning to identify anatomical landmarks in his plates and to properly interpret the evidences of disease. The authors have included a study of sinus development in infancy and childhood from the  $x$ -ray standpoint, and have demonstrated the wide variations from any fixed standards that may be readily shown at different ages.

H. K. P.

DIAGNOSE UND FEHLDIAGNOSE VON GEHIRNERKRANKUNGEN AUS DER PAPILLA NERVI OPTICI. By PROFESSOR DR. FR. SALZER, of Munich. Pp. 16; 29 illustrations in 2 colored plates. Munich: J. F. Lehmann.

THE author observes very justly that the ophthalmoscopist, perhaps even to a greater degree than he is himself conscious, is wont to control the objective appearances in the fundus, particularly choked disk and atrophy, by the history and subjective examination, both of which frequently fall away in psychic disorders, which latter are so often brought under his notice. The very fact that all the details are recognizable with such exactness with the ophthalmoscope adds to the difficulties of the situation. Uncertainty in objective diagnosis is due principally to two important circumstances: (1) The extraordinary degree of variability in the ophthalmoscopic picture of the normal papilla and its immediate surroundings, and (2) that the modifications of the picture occasioned by important pathological processes are frequently so slight.

Of the two excellent colored plates, the first containing 20 pictures taken from life, exhibits the great variability of the normal papilla. Eight pictures of the second plate are examples of pathological or doubtful findings. The variations indicated in both concern the color, outline, and relief of the papilla and the bloodvessels. The author insists that a diagnosis of either pallor or heightened color should only be made upon the basis of two or more examinations made at different times. A detailed description of each picture is given in the text. As a final justification the writer cites the lack of concordance in the statistics as to the percentage of pathological findings given by different observers in the same diseases. (Some of these divergences depend, of course, upon differences in the material.)

T. B. S.

---

THE BACILLUS OF LONG LIFE. A MANUAL OF THE PREPARATION AND SOURING OF MILK FOR DIETARY PURPOSES, TOGETHER WITH AN HISTORICAL ACCOUNT OF THE USE OF FERMENTED MILKS, FROM THE EARLIEST TIMES TO THE PRESENT DAY, AND THEIR WONDERFUL EFFECT IN THE PROLONGING OF HUMAN EXISTENCE. By LOUDON M. DOUGLAS, F.R.S.E. Pp. 163; 62 illustrations. New York and London: G. P. Putnam's Sons.

THIS volume is the twenty-ninth of the "Science Series" published by this firm. In each volume of this series a single author attempts to present his subject in a form at once accurate, scientific, and intelligible to the general reader. Certain volumes published in this series are well known and deserving of great praise, as, for example: *Fatigue*, by Mosso and others. The subject of the

present volume does not lend itself readily to this style of exposition, and the result has not been happy.

The first two chapters of the book are much the best, the first a short historical introductory account of the use of milk as a food, and the second, a description of the various fermented or soured milks used throughout the world. Both these chapters are filled with quotations, with references from works of travel and history which render them interesting.

The remaining chapters on the chemistry and handling of milk, the bacteriology of fermented milk, its preparation in the house and in the dairy, and finally, a consideration of the use of soured milk in health and disease, are of much less interest; especially is the section on the chemistry of the milk most unsatisfactory. It is unnecessary here to repeat the extravagant claims which have been made for soured milk, all of which the author faithfully includes.

On the whole, the book does not fulfil any purpose, and cannot be recommended.

O. H. P. P.

---

MODERN MICROSCOPY. A HANDBOOK FOR BEGINNERS AND STUDENTS. By M. I. CROSS and MARTIN J. COLE, Lecturer in Histology at Cooke's School of Anatomy. Fourth edition. Pp. 325; 113 illustrations. Chicago: Chicago Medical Book Co., 1912.

THIS is a book primarily for the man with a general interest in what the microscope will show of the world about him. At the present time, it must be acknowledged that this class is not a large one, and the societies which devote themselves to purely microscopical science are likewise much reduced in number. In the modern specialization of all science, the microscope has been treated more and more as a tool, and interest in it as an instrument has become subordinate to the various scientific branches in which it is used. It is the laudable effort of the authors to keep alive something of the old spirit and to direct interest outside of the narrow sphere of every-day work.

Part I comprises five chapters devoted to the microscope and its accessories. Part II consists of fifteen chapters, giving methods of examination of animal and vegetable tissues, including mounting of microorganisms, crystals, diatoms, etc. Part III, new in this edition, comprises special chapters by various writers, on the petrological microscope, rotifera, freshwater mites, mosses and liverworts, microscopy of foods, and other subjects.

This book cannot fail to be interesting to the beginner who wishes to master the principles and exact manipulation of the microscope or to anyone with the inclination and lesiure for a general study of Nature.

W. H. F. A.

UROLOGISCHER JAHRESBERICHT. Edited by DR. A. KOLLMANN and DR. S. JACOBY. On Literature of 1910. Pp. 460. Leipzig: Werner Klinkhardt.

THE editors, with the assistance of a large number of collaborators, have prepared a valuable volume, which permits a rapid review of the important papers, published in 1910, on affections of the urinary tract and on affections of the male genital system. The abstracts are grouped together into those on anatomy, physiology, pathology, and the chemistry of the urine. The great majority fall into the group under pathology, where they are further classified into those affecting the kidneys, ureters, bladder, etc. Some conception of the material represented in this review can be obtained from the fact that more than 1300 papers are abstracted, 319 under pathology, on the surgical affections of the kidneys and ureters. The volume is calculated to give, probably, as brief and at the same time as comprehensive a review of the literature of genito-urinary surgery for 1910 as could well be prepared.

T. T. T.

---

MANUAL OF PHYSIOLOGY. By H. WILLOUGHBY LYLE, M.D., B.S. (Lond.), F.R.C.S. (Eng.). Pp. 747; 137 illustrations. London: Oxford University Press.

THIS book covers, in a sufficiently comprehensive manner that which is required of a manual of physiology. The material is well selected and concisely and clearly described. Naturally, much which is found in the larger text-books, must be omitted in a work of this kind. However, by economizing space by omitting histology, except that absolutely necessary for purposes of description as well as embryology, and limiting the reference to experiments to a minimum, a proportionately large amount of purely physiological data is introduced in its 747 pages. Physiological chemistry receives a fair amount of attention, and some of the most used tests are described. The author has given such subjects as are of immediate value to medicine and surgery considerable space. For example, a chapter is devoted to inflammation, although, it is true, it is a short one. Elsewhere, too, we see frequent references to subjects of practical value to the clinician. But the book does not serve in any way as a guide to a laboratory course in practical physiology, nor does it intend to. This omission is wise, as much space is economized and then, again, books covering this field exclusively are now necessary for every medical student. As a manual, however, the book serves its purpose admirably.

E. L.

# PROGRESS OF MEDICAL SCIENCE

---

## MEDICINE

---

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

---

**Results of Antityphoid Vaccination in the Army in 1911, and its Suitability for Use in Civil Communities.**—FREDERICK F. RUSSELL (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1331) reports that antityphoid vaccination in the army has been carried out as follows: An avirulent culture of the typhoid bacillus is grown for twenty-four hours on agar, washed off in normal salt solution, standardized by counting the bacilli, killed by heating to 55° C. for an hour. Twenty-five per cent. tricresol is added as a matter of safety. This vaccine is injected subcutaneously in three doses at ten-day intervals. The first contains 5 million bacteria, the latter two a billion. As a rule, there is a local reaction consisting of a red and tender area about the size of the palm of the hand, subsiding within forty-eight hours. A severe general reaction occurs in only 1 to 3 persons per thousand. Since 1908, approximately 100,000 vaccinations have been made with no accidents. The effect on the morbidity from typhoid is now becoming apparent. From its use under conditions in the army, Russell believes that anti-typhoid vaccination in healthy persons is harmless and efficient, since it confers almost absolute immunity against infection under all conditions, assuredly for two and a half years, and probably longer. Thus the general vaccination of an entire community is feasible, and should be urged wherever the typhoid rate is high.

---

**Secondary Infections in Ulcerative Tuberculosis of the Lung.**—A. VEILLON and G. REPACI (*Annales de l'Institut Pasteur*, Paris, 1912, xxvi, 300) have studied the question of secondary infection in tuberculosis in the following manner: Smear preparations, animal

inoculations, and cultures on aërobic and anaërobic media were made from tuberculous sputum, cavities or lung tissue at autopsy, and from the circulating blood. By this method the cases studied fell into three groups. (1) A small number of cases in which no other organisms save tubercle bacilli were found. (2) A large number of cases in which the common aërobic organisms were found, never, however, in lung tissue or blood. Thus Veillon and Repaci think that such bacteria may remain in tuberculous cavities for a long time without causing complications. (3) A large number of cases in which anaërobic organisms were grown from sputa, cavities, and lung tissue. They consider this group of especial importance. In such cases clinically, the sputum is often colored and foul, giving to the breath a characteristic odor. Pathologically, in addition to tuberculosis, the lung shows evidence of putrefaction. Since these organisms penetrate deeply into the tissue, small areas of gangrene may appear, and by rupturing into the pleural cavity may cause a putrid pleurisy. On the whole, Veillon and Repaci believe that anaërobic infection gives to tuberculosis special features, characterized by foul sputum and gangrene of the lung with resultant aggravation of the patient's general condition.

---

**Aortic Aneurysm of Rheumatic Origin.**—P. EMILE WEIL and P. J. MÉNARD (*Bull. et Mém. Soc. méd. d. hôp. de Paris*, 1912, 3d, 491) describe a case of aneurysm of the ascending arch of the aorta, with aortic insufficiency, in a woman, aged forty-four years. There was no evidence of hereditary or acquired syphilis. The Wassermann reaction was negative. The family history was rheumatic, and when four years old the patient had suffered a severe attack of polyarticular rheumatism with subsequent less severe attacks every winter. From the facts that aneurysm, with typical clinical and radiosopic signs seemed to follow the rheumatism, and with history negative in other respects, it seems logical to consider the lesion of rheumatic origin. Doubtlessly, syphilis must be considered the most frequent cause of aneurysm. It is not the only one. From a careful review of the literature Weil and Ménard believe it is established both from pathological and histological standpoints: That aneurysms may develop after general infections, and rheumatism particularly. Clinically Weil and Ménard conclude that aneurysms of this etiology have essentially the following features: They develop in young people usually aged under thirty years, following one or more attacks of acute rheumatism. The most frequent location is on the ascending portion of the aortic arch accompanying a valvular lesion, usually aortic insufficiency. The outcome is rapid. [One wonders whether some of these instances of "rheumatic" aneurysms may not represent that remarkable dynamic pulsation of the elastic aorta sometimes met with in aortic insufficiency in the young.—W. S. T.]

---

**Mechanical Production of Fever.**—A. BOCK (*Archiv f. exp. Path. u. Pharmacol.*, 1912, lxviii, 1) has investigated the possibility of producing fever simply by mechanical irritation. All observations have been made on experimental animals. He arrives at the following conclusions: (1) The sodium ion has the specific property of raising body temperature. Intravenous injection of 20 c.c. of sterile Ringer's

solution has no effect on the temperature, while physiological salt solution practically always causes an elevation. (2) Injection of 20 c.c. paraffin suspension with a content of 0.01 to 0.1 per cent. of paraffin and 2000 to 11,000 particles of paraffin per 1 c.mm. regularly leads to elevation of temperature of  $\frac{1}{2}$  to  $1^{\circ}$  C. and more. (3) Injections of electrargol and electroplatinol produce fever. (4) Injection of Ringer's solution with 0.1 to 0.3 mg. arsenic per kilo of weight (rabbit) is followed by a rise in temperature. Fifty times this dose causes an immediate fall. (5). The fever following the injection of fine suspensions of paraffin, silver, and platinum may be due to a mechanical irritation of the sympathetic nerve endings in the vessel walls or to the action of products of metabolism of the leukocytes, which are formed as a response to the introduction of the foreign material.

---

**Experimental Digestive Leukocytosis.**—M. BRASCH (*Zeitschr. f. exp. Path. u. Therap.*, 1912, x, 381) approaches the question of digestive leukocytosis, about which there has never been unanimity, from the experimental side. He records numerous experiments on rabbits and dogs and finds that a digestive leukocytosis follows the taking of food during hunger practically without exception. The kind of food seems to be of minor importance, as it was observed to occur after giving nucleic acid, protein, fat, and carbohydrate. The leukocytosis appears within four to ten hours after the food is given. In rabbits it is generally the small lymphocytes which are particularly increased, though at times there is a uniform increase in all varieties of leukocyte. In the dog, on the other hand, the latter condition is found, or there is a leukocytosis due to increase of neutrophilic polynuclear cells. The digestive leukocytosis is not to be considered as a protective reaction of the organism, such as one observes after injection of foreign matters into the body.

---

**Paroxysmal Ventricular Tachysystole of Psychic Origin.**—K. KURÉ (*Deutsch. Arch. f. klin. Med.*, 1912, cvi, 33) reports the study of an eleven year old girl with tachycardia due to ventricular extra-systoles. The attacks were brought on by psychic irritation. Analysis of simultaneous tracings of veins, artery, and heart apex demonstrated the fact that the condition was essentially a ventricular tachysystole which was quite independent of auricular rhythm. Whether in this case the ventricular tachysystole was due to heterotopic native impulses in the ventricles or whether it arose through an increase of the irritability (*Anspruchsfähigkeit*) of a certain part of the ventricle is not clear. It is, nevertheless, highly probable that in this cases the extra-systoles are attributable to stimulation of the accelerans. As a result of the ventricular tachysystole, a complete dissociation was produced temporarily. Kuré suggests that a part of the cases of paroxysmal tachycardia are due to ventricular extrasystoles. [An observation which has been made by many students.—W. S. T.]

---

**The Chemistry of Tuberculous Sputa.**—R. EISELT (*Zeitschr. f. klin. Med.*, 1912, lxxv, 71) has studied tuberculous sputa particularly with reference to their enzymatic activities. The methods of examination are described in detail. He finds that the proteolytic enzyme usually

present in tuberculous sputa is a tryptase, but it is by no means so constantly present as has been supposed heretofore. Frequently tryptase alternates with antitryptase in the sputum. Usually this is the case during febrile periods. Like pancreatic trypsin, the tryptase of the sputum, activated with calcium salts, has plastein-forming activity, which is retained in the presence of antitryptase. Lipolytic enzymes were not demonstrable. The proteolytic activity varies inversely with the coagulable protein of the sputum and directly with the quantity of albumoses and amino-acids. Chemical examination of tuberculous sputa showed that of all inflammatory lung diseases tuberculosis is associated with the highest values for coagulable protein. Albumoses are also more abundant than in other diseases. Peptones, on the other hand, are present only in traces; it is probable that they are absorbed almost as rapidly as formed. Of other nitrogenous bodies, the large quantity of incoagulable nitrogen (Rest-N) is striking. It is chiefly in the form of glycosamine and amino-acids.

---

**Adrenalin in Pathological Sera.**—STEWART (*Jour. Exper. Med.*, 1912, xv, 547) attempted to demonstrate adrenalin in the sera of blood obtained by venesection from 14 patients suffering with different maladies among which were malignant Graves' disease, myxedema, chronic nephritis, arteriosclerosis, angina pectoris, syphilis, general paresis, gout, and pneumonia. For detection of adrenalin in blood serum Stewart suspended rabbit intestinal and uterine segments in Ringer's solution and measured the increase in the size of the beats and the degree of muscle tone when the medium was replaced by the serum in question. No one of the pathological sera yielded evidence of the presence of adrenalin. This result is explained by Stewart's experimental work. Serum from the adrenal veins of the dog collected with the least possible disturbance gave a negative reaction. Whereas in serum collected during mechanical stimulation of the gland the reaction was distinctly positive. Stimulation of the splanchnics changed a negative reaction to positive in serum of blood from the inferior vena cava, draining the adrenal and lumbar veins. The general admixed blood of the inferior vena cava and elsewhere more distant in the general circulation failed to show the presence of adrenalin whether the splanchnics were stimulated or not. The cause of the negative result is without doubt the high degree of dilution in the inferior vena cava of the blood coming from the adrenals, greater than a dilution of 1 to 1,000,000 as measured by this method.

---

**Malarial Pigment and the Malarial Paroxysm.**—BROWN has shown that the pigment elaborated from the hemoglobin of the red blood corpuscle by the malarial parasite and liberated into the circulation of the host at the time of segmentation of the parasite is undoubtedly hematin. In his work upon hematin metabolism he noted that a rabbit receiving an intravenous injection of this pigment developed a very pronounced shaking chill strikingly like that of malaria. With the hope of finding in this substance one of the hypothetical toxins operative in malaria Brown (*Jour. Exper. Med.*, 1912, xv, 579) undertook a series of ninety observations upon the effect of the intravenous injection of alkaline hematin in rabbits. The hematin used was derived



from rabbit, dog, and ox blood, the effect being the same in each instance. After careful previous records of temperature, and observations of the effect of the alkaline medium, the injections in question were made intravenously. Simple calculation on the basis of 4.47 per cent. hematin in hemoglobin and a 1 per cent. (at least) infection of the red blood corpuscles would give 3.7 milligrams of hematin per kilo of body weight as the amount liberated in an average paroxysm of malaria. Brown's dosage was from 1.3 milligrams to 28 milligrams per kilo of body weight, corresponding roughly to an injection of 0.3 to 7.5 per cent. of the red blood corpuscles. Without exception every dose of hematin administered elicited a definite temperature response. Within certain limits the extent of temperature elevation was proportional to the amount of hematin injected. Even other features suggest a malarial paroxysm. After a short period of restiveness the temperature rises and the animal's skin becomes pale, cyanotic, and cold. There is even shivering. This stage of chill lasts an hour and is terminated abruptly by a dilation of the superficial vessels, the ears becoming flushed and hot. This coincides with the initial drop and the duration of temperature above normal. In a word the injection produces a paroxysm characterized by a short prodromal stage, a stage of chill and rise in temperature, and a hot stage, identical in details with the corresponding ones in the paroxysm of human malaria. In the estimate of Brown, the pigment hematin as liberated by the malarial parasite into the circulation of the human host is at least a potentially toxic substance.

---

**Albuminuria and Cylindruria.**—BARRINGER and WARREN (*Arch. Int. Med.*, 1912, ix, 657) have studied the question of the significance of albumin and casts in the urine of apparently healthy men. The material at their disposal were the records of 396 men examined for life insurance ten years before. As far as ordinary physical examination could determine, they were normal at that time except for the presence in the urine of serum albumin with or without casts. They were divided into three groups, as follows: 115 showed simple albuminuria; 203, albuminuria and a few hyaline casts; 53, albuminuria and a few granular casts. The incidence of albumin and of granular casts increased with each decade, but the decade-incidence of the hyaline-cast groups was almost equal. Ten years after these records, 70 of the original list were visited and examined. No one of 20 in the group of simple albuminuria had interstitial nephritis. In 8 the same condition persisted, 30 of the men had showed albumin with hyaline casts. One of these had developed nephritis, in comparison to 2 of the group with albumin and granular casts. Two in the second group and 5 in the third were doubtful. In the entire series of 70 men, 38 were free from cardiac or renal disease. Three surely and 7 possibly have chronic interstitial nephritis, 22 still show the same urinary condition as they did ten years ago. The mortality of the original group was decidedly high, 25 instead 16 as it would have been computed for men free of albumin and otherwise normal. The absence of nephritis shown in the 20 cases of simple albuminuria, after ten years, and the low mortality in this group from renal and arterial disease indicate that it is exceptional for the albuminuria of young adults to become a symptom of incipient nephritis.

## SURGERY

---

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA  
AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON  
TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE  
UNIVERSITY HOSPITAL.

---

**The Influence of an Aseptic Serous Inflammation upon the Dissolution of Catgut.**—CALLAM (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 265) says that an aseptic serous inflammation delays the dissolution of catgut in the mouse, an animal which absorbs the thread very quickly in the presence of severe suppuration. In the cases where the reaction on the inserted catgut is slight, as in the guinea-pig, no effect could be shown. The results of his experiments show that an artificial inflammation delays the absorption of catgut in the body of the white mouse. The uninfluenced process is nothing more than an aseptic suppuration. This process is moderated because the edema, caused by the artificial aseptic inflammation, scatters the leukocytes and permits only a slow development of their contained digestive strength. The tissues, therefore, which are subjected to the peptic influence, as well as the catgut, undergo less damage. Callam, in this way, coincides with the view of Bier, that the inflammation and its inherent healing power serve to moderate the damage done by the exciting cause of the inflammation. Since, as Joseph says in his text-book on hyperemia treatment, the slower and more mild the abnormal chemical process set up by the inflammation, attacks the surrounding tissue, the more time the tissue has to guard itself against the hurtful influence and to prevent the threatened field from damage and destruction. The flames which scorch the flesh of the unfortunate one in a few moments, allows the body no defence. So with the summer sun, which burns the body during weeks and months. The bacterial inflammations act in a similar manner. We have here a scientific explanation for the fact, discovered empirically, that catgut impregnated with antiseptics are destroyed more slowly than the catgut without antiseptic impregnation. When the inflammatory irritation does not cause edema of the tissues in which the catgut lies, the aseptic leukocytosis can develop more quickly and digest the catgut and tissues.

---

**An Experimental Contribution Concerning the Formation of Bone from the Injection or Implantation of Periosteum Emulsion.**—JOKOI (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 433), following the work of Nakahara and Dilger in the production of bone formation, carried out their experiments, chiefly on rabbits, rarely on dogs. They

removed periosteum from the tibia and with sharp instruments divided it into small pieces. These were implanted subcutaneously or in the muscles. After varying periods they were cut out of the tissues and examined. From autoplasmic implantation or injection of periosteum emulsion, Jokoi could, in 6 out of 7 experiments, produce a more or less marked bone formation. The active bone formation depends, above all, upon the mechanical relations of the implanted or injected pieces of periosteum to the surrounding tissues. In the unsuccessful experiments these were always shrivelled up or rolled together. In one of the experiments he established that the new-formed piece of bone had not undergone any absorption, but had shown rather a tendency to wider extension. From homoioplastic implantation or injection of periosteum emulsion also, bone formation can be produced, although not so frequently or so markedly as from the autoplasmic. From heteroplastic implantation or injection of periosteum emulsion, no bone formation could be produced. The associated injection of fresh blood of the same animal appeared to have no favorable influence upon the osteoblastic activity of the transplanted pieces of periosteum. In all the experiments the associated particles of bone underwent lacunar absorption.

---

**Small Plastic Operations on the Fingers and Hands.**—KLAPP (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 479) reports several ingenious operations to make the hand more useful after injuries. When a finger has been cut off and the cut surface is even, it has usually been necessary to remove a piece of the phalanx in order that the end of the bone could be covered by the skin and underlying soft tissues. This sacrifices some of the length of the finger and increases the loss of function seriously, particularly in certain occupations, as in physicians and piano players. In one case in which the end of a finger had been cut off obliquely at the level of the middle of the finger-nail, a palmar flap having a lateral attachment was made and carried over the end of the bone, its free end being sutured in place on the opposite side of the finger. When the cut is transverse, by a transverse incision on the palmar side a short distance from the cut margin of skin, a flap can be made which is attached on both sides. This can be drawn by sutures as a bridge of tissue over the end of the bone. In a case in which the thumb was entirely removed, even with the side of the hand, Klapp separated the metacarpal bone of the thumb from the rest of the hand by dividing the soft tissues between. Two skin flaps were formed, one from the palmar and the other from the dorsal side. The interossei muscles were then divided, and one skin flap was used to cover the raw surface on the thumb side, while the other flap was made to cover the raw surface on the hand side. In this way the patient was given a short but very useful stump for a thumb. An illustration shows the repaired hand grasping the handle of a mallet, the improvised stump of the thumb seeming to add much to the firmness of the grasp.

---

**The Clinical Utilization of the Coagulation Time of the Blood in Jaundice.**—KUNIK ( *Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 574) says that the taking of the coagulation time of the blood is rarely used in practical medicine because the methods thus far employed are not

easily carried out. He believes the Kottmann method is easy of performance and very reliable. In many patients jaundiced from gallstone disease, the clotting time is normal, and there is no inclination to hemorrhage. In very grave cases of jaundice in which there is a tendency to hemorrhage, the ability of the blood to clot is very much lowered. This is independent of the intensity of the jaundice. When in patients with jaundice, who come for operation, an examination shows a retarded clotting time of the blood, we may assume the existence of an advanced stage of a liver affection, which renders the case no longer suitable for operation. The examination of the coagulation time of the blood has a diagnostic and prognostic value for the practical physician, and especially for the surgeon, since it permits him to avoid a dangerous operation. It is also an important aid for the differential diagnosis of jaundice.

---

**The Surgery of the Deep Pelvic Lymph Nodes.**—KOTZULLA (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 55) says that the surgery of the deep pelvic nodes is concerned chiefly with malignant degeneration and tuberculosis. In malignant disease we can limit the extirpation to the inguinal region only in the beginning of the disease. In every other case, that is, whenever there is only a slight suspicion that the disease has already advanced, it becomes necessary to lay open the femoral canal, and after dividing Poupart's ligament to investigate the suprafemoral nodes. If these are diseased we should proceed further. In tuberculosis a radical procedure is also necessary. In general an excision of the superficial nodes should be done only when the disease is actually limited to these, in all other cases a radical operation being necessary. It is to be admitted that an indiscriminating search for the deep pelvic nodes is to be avoided, in view of the considerable danger of lymph stasis and chronic edema of the extremity. In the absence of contraindications, the exposure should include the suprafemoral or deeper nodes. The chief contraindications will be: The existence of generalized tuberculosis, the simultaneous existence of disease of vital organs, and the invasion of the more centrally located groups of nodes which are not surgically accessible. The age and general condition of the patient are also to be considered. The operation of choice is that of Sprengel. He extirpates the usually diseased inguinal nodes by means of a longitudinal incision, and lays the femoral vessels free to Poupart's ligament. In order to have a free exposure and to command the anatomy of this region so as to avoid untoward accidents, the ligament is divided opposite the vessels. By an oblique incision along Poupart's ligament the reflection of the peritoneum is exposed. By elevation of the pelvis the peritoneum is carried backward so that the nodes and large vessels are exposed. Now follows the extirpation of the nodes under continuous control of the vessels up to the bifurcation of the common iliac vessels. The wound is partially closed by sutures and the rest by gauze packing. The prognosis of the operation is relatively favorable. While it is extensive the shock produced by it is relatively slight. None of the patients died during or at the end of the operation. The further prognosis, especially in malignant disease, depends naturally upon the extent of the disease. The cases which are in the beginning stages

of the disease promise a good permanent result. If, however, the deep pelvic nodes are already involved to a considerable degree, the prognosis will vary with the grade of the disease. Such cases will probably be excluded ultimately from those suitable for operation. The prognosis in tuberculosis is generally favorable.

**Statistical Contribution Concerning the Result of the Wilms Method of Treating the Stump in Resection of the Stomach.**—KUNIKA (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 483) describes the technique as follows: A median incision is made, beginning at the xyphoid cartilage. The pyloric portion of the stomach is brought forward as far as possible, and the extent of the tumor, the lymph-node involvement, and the adhesions are established. The gastrosplenic ligament is now divided, after double ligation of its vessels. The nodes in the gastrosplenic ligament remain attached to the stomach. The separation will be carried in the direction of the duodenum as far as the enlarged nodes extend, or otherwise a thumb's breadth beyond the tumor. The upper portion of the duodenum is also isolated on all sides. The lesser omentum is divided beyond the palpably enlarged nodes between clamps or ligatures. The exposure must extend considerably further on the cardiac side than on the duodenal. Then follows the division of the duodenum. A strong closing suture is applied in the pressure groove made in the duodenal stump by the clamp, and is tied. This with the stump is inverted by one or two purse-string sutures. After the turning in of the stump the ligation closing it is removed. The gastric stump will then be closed in its upper half down to the opening left for anastomosis, which will be united to one in a coil of the jejunum passed through an opening in the mesocolon. The wall of the small intestine at the anastomosis is made to cover some of the sutures closing the divided end of the stomach for a short distance above the anastomotic opening. This strengthens the weakest place in the anastomosis. The afferent limb of the anastomosed loop of the jejunum is fixed to the margins of the opening in the mesocolon by several sutures to prevent later ileus from the passing through the opening of another coil of intestine. After the usual cleansing of the field of operation, and covering of the sutures with omentum, the abdominal wound is closed in layers in the usual way. Fourteen cases operated on in this way by Wilms are reported. All but one left the hospital well, this one dying of an intercurrent pneumonia.

**A Study of Vesico-intestinal Fistulæ.**—PRISTAVESCO (*Jour. d'Urol.*, 1912, ii, 321) says that acquired vesico-intestinal fistulæ constitute a rare affection. They can be divided into three categories, according to the segment of the digestive tube in communication with the bladder and according to their characteristics: (1) Those between the bladder and the rectum, and large intestine in general. (2) Those communicating with the acquired intestinal diverticula with a predilection for the sigmoid colon. (3) Those communicating with the appendix, ileum, or colon. Of the three kinds, the diverticulo-vesical fistulæ are the most rare, their proportion being about 2 per cent. All varieties have their origin in common causes, that is, they may be due to trauma, inflammation, cancer, and tuberculosis. More

rarely they may be due to actinomycosis or syphilis. The symptoms, aside from those of the causal affection, are the emission of gas, fecal matter, or alimentary debris by the urethra, and the escape of urine by the anus. Later are added those of secondary infection, and the constitutional symptoms. The diagnosis of recto-vesical fistula is made by the recognition, by the rectal touch or rectoscopy, of the fistulous orifice. The diagnosis of the appendiculo-vesical variety is made more certain or probable when it is preceded by an appendicitis. The diverticulo-vesical can only be suspected in patients suffering from disease of the heart or liver with edema, and in those in whom one establishes a painful swelling in the left iliac fossa. One can only make conjecture as to whether the abnormal communication is direct or indirect. In the female it is nearly always indirect. The prognosis of vesico-intestinal fistulæ is grave. The average duration of life, according to Pascal, is three years. The treatment should be preventive in the cases in which the fistula is threatened, and it is directed to the diseased organs (bladder, intestine, or neighboring organs) to guard against the fistula formation. The treatment will be palliative in inoperable cases (tuberculosis, cancer, etc.). Medical treatment, local, and general, should always be employed in cases of vesico-intestinal fistula to prevent infection along the ureter to the pelvis and kidney. It will be preparatory to operation and will aid in the cure of cases operated on. The surgical treatment consists in the removal of the abnormal communication. For this purpose several paths have been tried, but the best, according to the results obtained, appear to be the peritoneal and transvesical.

---

**Treatment of Dislocation of the Head of the Radius Complicated by Fracture of the Ulna.**—ASHHURST (*Annals of Surgery*, 1912, lvi, 631) says that in recent cases reduction of the dislocated radial head should be secured, by arthrotomy and capsulorrhaphy if necessary. As Kirmisen says, in such injuries the dislocation is everything, the fracture nothing. When reduction is secured the fracture almost invariably falls into good position. If it does not, it may be fixed by suture or plate. In old cases with the ulna united, attempt reduction of the dislocation by arthrotomy, and retain the radius in place by capsulorrhaphy. If reduction after arthrotomy proves impossible, as it may if the ulna has united in bad position, it is better to excise the head of the radius than to interfere with the ulna, unless the deformity in the ulna is extreme. In such cases osteotomy of the ulna may be done. In old cases with non-union of the ulna, expose the ulna fracture first, and after freeing the fragments, secure reduction of the dislocation (by arthrotomy if necessary, including capsulorrhaphy); then treat the ulnar fracture as if no dislocation had existed. In cases with musculospiral paralysis, excision of the radial head failed to secure a good result in 1 case (Zschock), and there is no evidence that reduction and capsulorrhaphy would not have been successful in two others (Albertin, Kammerer) in which excision was done.

## THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS,  
COLUMBIA UNIVERSITY, NEW YORK.

**The Treatment of Syphilis with Neosalvarsan.**—WOLFF and MULZER (*Münch. med. Woch.*, 1912, lix, 1706) report their results with the use of neosalvarsan in 30 cases of syphilis. They conclude that neosalvarsan is far less powerful than salvarsan as a specific for syphilis even when used in larger quantities, and that it is far more dangerous. They warn particularly against its use in ambulant patients. The toxic effects observed were as follows: A chill in 1 case; Herxheimer's reaction in 3 cases; headache, vomiting, and diarrhea in 14 cases; extensive drug eruptions in 4 cases; herpes labialis in 2 cases; nephritis, paralysis, and other severe symptoms in 1 case.

**Experiences with Neosalvarsan.**—KALL (*Münch. med. Woch.*, 1912, lix, 1714), upon the basis of 39 cases of syphilis treated with neosalvarsan, warns against frequent repetitions of injections because he observed severe toxic effects following the use of neosalvarsan in this way. He also condemns the recommendation that ambulant patients be treated with neosalvarsan.

**The Treatment of Gout with Atophan.**—BACH and STRAUSS (*Münch. med. Woch.*, 1912, lix, 1714) report 19 cases of gout treated with atophan in doses of 0.5 gram combined with sodium bicarbonate, 5 grams, at four-hour intervals for three-day periods. These periods of atophan treatment were followed in every instance by an increased uric acid excretion to double that existing before the treatment. Usually the increase in the uric acid was noted on the first day of the administration of atophan. The withdrawal of the remedy was followed by a decline of the uric acid excretion below the normal that slowly rose to its former level. The administration of the remedy gave rise to no kidney irritation and no increase in the amount of the urine. In fact 2 patients with contracted kidneys bore atophan without any untoward symptoms and with no change in the urinary findings regarding albumin and casts.

**The Treatment of Diphtheria Carriers by Overriding with Staphylococcus Aureus.**—LORENZ and RAVENEL (*Jour. Amer. Med. Assoc.*, 1912, lix, 690) report their results with reference to ridding the throats of diphtheria bacilli by means of a staphylococcus aureus spray. In all 17 patients received this form of treatment. Three were carriers, pure and simple, never having shown local or general symptoms of diphtheria. Six patients had clinical symptoms of diphtheria, but persisted as carriers long after convalescence had been established.

In 8 cases the staphylococcus spray was used early in the course of the diphtheria. The preparation used was a fresh suspension of the *Staphylococcus pyogenes aureus* in normal saline solution or a bouillon culture twelve hours old. The spray was given at a temperature of 96° F. Sufficient was used to make the pharynx "dripping wet" and the nasal cavities were sprayed until the liquid ran down the back of the throat. They advise a combined nasal and throat spray, to be given at four-hour intervals on two succeeding days; the first swab for examination should be made the third day. The best results were obtained in the diphtheria bacillus carriers. In 2 cases negative reports were received after six applications of the spray, and in the third after nine applications. Four other cases cleared up within one week, but on the other hand one required six weeks and another fifty days of treatment before the throat was freed of diphtheria bacilli. Lorenz and Ravenel believe that in those cases where the spray was used early in the course of the disease, better results were obtained in those patients treated with the staphylococcus spray than in those treated by the ordinary antiseptic applications.

---

**Vaccination for Typhoid by Living Sensibilized Bacilli Typhosi.**—BROUGHTON-ALCOCK (*Lancet*, 1912, clxxxiii, 504) draws the following conclusions from his observations as to the effect of vaccination with sensibilized typhoid bacilli. (1) The successful experiments on man by the method of Besredka have taken us one step forward in the application of vaccination. Cannot the sensibilized living *Bacillus typhosus* be considered in the same light as the virus of smallpox, attenuated or modified by the immunized calf-lymph, and which gives rise to a specific immunity that may be verily called ideal? (2) The sensibilized living bacilli remain alive over four months without exceptional precautions, and their preparation is simple, rapid, and practical. (3) The first dose for a woman of average size should be 500,000,000 sensibilized living bacilli in 1 c.c. of 0.8 per cent. saline. For a man of good physique the first dose should be 750,000,000 in 1 c.c. of 0.8 per cent. saline. The second dose, seven to nine days later, should be double these quantities. The dose of 500,000,000 represents 1 c.c. of a culture of twenty-four hours on gelose without peptone in 100 c.c. of saline. Diluted 1 to 40 and at the dose of 0.1 c.c. it fixes 0.1 c.c. of titrated guinea-pigs complement. (4) There is no general reaction and only an insignificant local reaction following these injections. The patient is in no way obliged to change his daily routine of living. These results are in marked contrast with Broughton-Alcock's experience of the reactions following the injections of the same number of killed bacilli in the vaccine of Wright-Leishman. An elevated temperature, a previous history of typhoid, and the time of menstruation are not contraindications to the giving of the living sensibilized *Bacilli typhosi*. (6) The sera of persons injected with sensibilized *Bacilli typhosi* have not been found to deviate complement and only rarely to agglutinate an emulsion of a young culture. Their addition, however, markedly increases phagocytosis. Probably they also contain anti-endotoxin bodies. (7) The detected presence of specific amboceptors, agglutinins, bacteriolysins, cannot be said to show the degree



of immunity attained. The results of experiments in vitro cannot be interpreted as denoting the state of the patient's resistance. (8) As it has been asserted by all authors that vaccination by living micro-organisms is the most effective, and, moreover, this has been proved by the experiments on chimpanzees made by Metchnikoff and Besredka, and as Broughton-Alcock's observations on man have proved the innocuousness of the living sensibilized *Bacillus typhosus*, he presumes to conclude that this method ought by preference to be applied to man. Since the writing of this article 750 persons, including many soldiers, have been inoculated. The results are most satisfactory and encouraging.

---

**Hexamethylenamin in the Treatment of Systemic Infections, with a Special Emphasis upon its Use as a Prophylactic.**—CROWE (*Johns Hopkins Hospital Bull.*, 1912, xxiii, 255) says that the suggestion that hexamethylenamin be used in the treatment of systemic infections is based entirely upon the results of experimental and clinical observations. He believes that it is of value not only as a therapeutic, but especially as a prophylactic measure in a great variety of maladies. Among the conditions which may be favorably influenced by the administration of hexamethylenamin the following are the most important: (1) Infections of the genito-urinary tract and typhoid bacilluria; (2) infections of the bile-ducts and gall-bladder; (3) infections of the cerebrospinal system, poliomyelitis, epidemic meningitis, meningeal infections following injuries or infectious processes elsewhere in the body; (4) infections of the respiratory tract, including infections of the paranasal sinuses and ears, acute rhinitis, acute tonsillitis, and some forms of bronchitis. In lobar pneumonia and pulmonary tuberculosis it is doubtful whether this drug is of any value. Hexamethylenamin, given either by mouth or by rectum, makes its appearance in the bile and in the urine almost simultaneously. Provided large doses of hexamethylenamin are given, at least 75 grains a day, this drug appears in the gall-bladder in a concentration which suffices to render the bile an unsuitable media for the growth of bacteria. Since 1908 it has been a routine measure in the Johns Hopkins Hospital to administer hexamethylenamin in all cases in which a meningeal infection is a possible or threatened complication. There have been 20 cases of compound fracture of the vault, similar in that there was a laceration of the meninges and underlying cortex in each instance. In 8 of the earlier cases hexamethylenamin was not given, and the mortality from infection was 50 per cent. To each of the remaining 12 cases, hexamethylenamin was given immediately after the injury, and at frequent intervals, until all danger of infection was past. Ten of these patients recovered, while 2 succumbed with a pneumococcal meningitis. In 40 cases of hypophysis tumor operated upon, hexamethylenamin has been administered as a prophylactic measure. It was given in doses of from 40 to 60 grains during the twenty-four hours preceding the operation, and even larger amounts for several days after the operation. In 31 cases there were no postoperative complications whatever. In 9 cases there were symptoms suggesting a meningeal infection. Three of these patients finally succumbed to

meningitis; the other 6 patients recovered. They have abandoned the custom of giving this drug in doses of 10 to 15 grains at stated intervals, since it is often difficult to induce the patient to take the 250 or 300 c.c. of water in which doses of this amount should always be dissolved. In very ill patients, the drug is usually administered by rectum, from 50 to 100 grains being dissolved in a liter of salt solution, and allowed to flow into the bowel a drop at a time. There has not been the slightest evidence of undue irritation of the intestinal mucosa, even after one or two weeks of almost continuous administration by this method. If the patient is able to take nourishment by mouth, from 2 to 3 grains of hexamethylenamin are added to every ounce of liquid, and it is often possible in this way to give from 60 to 100 grains a day without the patient's knowledge and without producing gastric or renal irritation. There have been but very few instances in which toxic symptoms have resulted from the administration of large doses of hexamethylenamin, although from 200 to 300 grains daily for four or five days were given; even in children, doses of 100 or 125 grains a day have produced no irritative symptoms. In 95 cases in which the average dose of hexamethylenamin was 75 grains a day for ten days, painful micturition and hematuria occurred in 7 instances. Three of these cases were fatal meningelial infections, and the drug was given in unusually large amounts with the hope of checking the progress of the disease. At the post mortem examination it was apparent that the hematuria had its origin from the mucous membrane of the bladder, and was not due to an acute renal irritation. In the remaining 4 cases the urine rapidly became normal on the withdrawal of the drug. Crowe says that in a few persons very susceptible to the drug, even a small dose may give rise to skin rashes, catarrh of the mucous membranes, gastric or urinary irritation. However, this fact does not invalidate the use of the drug. He believes that untoward symptoms usually arise as a result of insufficient dilution, and such symptoms have invariably disappeared on withdrawing the drug and producing active diuresis by forcing liquids.

---

**The Crotalin Treatment of Epilepsy.**—SPANGLER (*New York Med. Jour.*, 1912, xcvi, 520) adds to previous communications on this same subject. Since first using the venom in the treatment of epilepsy (March, 1909), he has used it in 109 cases, and has given to these patients over 2000 injections of the venom without untoward effects. He gives a *resume* of the results in 6 of the 11 cases first reported that he has since kept under observation. Five of these patients have been free from convulsions for periods of from seventeen months to three years and three months. One patient who formerly had from two to five major convulsions each week now only has one attack every three or four months, and physically and mentally has made such improvement that he can work regularly at his employment. Crotalin solution is made from the dried, yellowish crystal-like scales of the evaporated venom of *crotalus horridus*, the rattlesnake. The venom is obtained from the living reptile and dried between glass plates, under a bell jar, in the sun. The crystals are dissolved in glycerin and sterile water; to which a few drops of tricresol are added as a preservative. The solution is standardized and given by hypodermic injection. Spangler

believes that the venom treatment is indicated in many of the essential cases of epilepsy. He says that not only are the virulence and number of epileptic convulsions favorably influenced by the crotalin treatment, but the excitability of the nervous system is modified and the general health of the patients, their mental facilities, and metabolism in every respect are considerably improved. The quality of the blood, and possibly its chemical composition seem to be affected by the injection of the venom. As to the exact effect it has on the coagulability of the blood, further observation is necessary. There is no danger in the use of crotalin as long as the necessary aseptic precautions are taken in its administration and the treatment is carried out with careful observation as to its effect on the patient.

---

**Further Experiences of the Specific Curative Action in Amebic Dysentery of Hypodermic Injections of Soluble Salts of Emetin.**—ROGERS (*British Med. Jour.*, 1912, 2695, 405) believes that emetin salts administered hypodermically in sufficient doses will kill amebæ in both the intestinal and liver abscess walls. With regard to dosage he says that either the hydrochloride or the hydrobromid of emetin are equally useful, the former being the more soluble, while the latter requires about 2 c.c. of sterile water or saline to dissolve it. At first Rogers chiefly used  $\frac{1}{3}$  grain doses, but now very seldom employs less than  $\frac{1}{2}$  grain at a time, and often gives as much as  $\frac{2}{3}$ , the equivalent of 60 grains of ipecacuanha, and has twice injected 1-grain doses subcutaneously without any vomiting or depression, but such a quantity is only required in extremely acute amebic dysentery. Rogers says that the extraordinary rapidity with which marked improvement follows the subcutaneous injections of  $\frac{1}{2}$ -grain doses of emetin is of the greatest diagnostic importance for cases of bacillary dysentery, and that other non-amebic causes of the presence of blood and mucus in the stools are not materially affected by the drug, although it has done no harm in them. In Rogers' experience, whenever active amebæ of the histolytica type, including the variety described by Noc and shown by Greig to be the common one in India, have been found in dysenteric stools, the disease has eventually proved amenable to full doses of ipecacuanha, if not too acute or far advanced. Rogers gives details of a few cases of amebic dysentery and amebic abscesses of liver and spleen treated by this method with good results.

---

## PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,  
OF PHILADELPHIA.

---

**Serous Meningitis and Associated Conditions in Childhood.**—KURT BLÜHDORN (*Berlin. klin. Woch.*, 1912, xlix, 1796) reports a study of 11 cases of serous meningitis. This term is used to designate the

external form of the disease in which there is an increase of fluid in the subarachnoid space, due to an inflammation of infectious origin. A serous meningitis can be caused by the typhoid bacillus, the pneumococcus, the bacillus of influenza, the meningococcus, and especially by the streptococcus originating in the ear. While a serous meningitis may be merely the fore-runner of a purulent meningitis, and may cause death in the first instance without apparent pathological change in the tissues, yet there do occur pure cases of serous meningitis in which the fluid remains clear and these cases almost invariably recover. Blühdorn believes that in some cases the substances elaborated by the bacteria, through chemical action on the brain cells and surrounding tissue, excite the plexus to hypersecretion. Independently of primary serous meningitis, there occur similar meningeal conditions during pneumonia and pertussis in which no bacteria can be found in the spinal fluid by the most careful bacteriological tests, both cultural and animal. Therefore, it is assumed that this specific factor of the primary disease or its toxin is the etiological factor of the meningitis. Blühdorn's cases all showed the general symptoms and course of a meningitis with an increased quantity of clear spinal fluid under pressure of more than 12 to 15 cm., which in children can be considered pathological. The result of the lumbar puncture showed invariably an absence or at most a slight trace of albumin, very few formed elements when present at all, and no bacteria under the most careful tests. Rigidity of the neck and Kernig's sign in children aged under three years are difficult to determine, as is also the bulging of the fontanelles. Three cases of serous meningitis were associated with a pneumonia. One of these cases ultimately developed pus in the spinal fluid which showed also the pneumococcus. The other 2 cases remained clear types of serous meningitis undoubtedly actuated by the bacterial toxins only. Two cases of serous meningitis developed during pertussis, where the actuating factor may have been either the pneumococcus or the specific organism of pertussis. Five cases are discussed in which there was no primary disease present to explain the meningitis and in which the spinal fluid was sterile although under high pressure, and at times showed a trace of albumin and a few lymphocytes. Lumbar puncture in many of those cases had a beneficial effect on the acute condition, although several cases subsequently showed mental impairment.

---

**Icterus Simplex in Childhood.**—ALBERT NIEMANN (*Med. Klin.*, 1912, viii, 1624) prefers the name icterus simplex because no proof of an infectious etiological factor has appeared, although the onset and course of the disease gives one the impression of an infectious condition. Icterus simplex is common in childhood, and several observers have reported from 50 to 73 per cent. of cases as occurring in children during a general outbreak of the condition. In Berlin, however, the average occurrence in children seems to be 1 per cent. of all cases of icterus. Niemann bases his article on a series of 130 cases. The majority of cases follow a mild type, clinically, with a short duration of about one week and usually no symptoms, except the icterus of the skin and sclera, and icteric urine. Occasionally there occur anorexia, coated tongue, or vomiting. The feces are usually normal. The

other type of case exhibits prodromal-like symptoms of fever, headache, dizziness, chills, anorexia, nausea, and vomiting. This type of attack simulates more closely a general infection, especially since a number of days elapse before the appearance of icterus, and, as a rule, the gastro-intestinal symptoms do not develop. Enlargement of the liver was a rather frequent symptom in this series, but disappeared with the fading of the icterus. A slowing of the pulse was rarely observed. In a very small group of cases the disease was protracted over weeks or even months. In this class the gastro-intestinal symptoms were especially marked, the icterus more intense and lasting, and the liver was swollen to a marked degree. Practically all authorities agree that this condition is found most prevalent in the fall months and many observers refer to epidemics of this disease in the Fall. In Niemann's cases 55 per cent. occurred in the months of October and November. This fact, with the occurrence of a number of cases in the same family, especially among sisters, is an argument in favor of an infectious etiological factor. The disease rarely affects children aged under two years, and the greatest number of cases occurred between the seventh and eighth year. Niemann found a fat-free diet unnecessary, of no therapeutic value, and accompanied by marked loss of weight. A moderately fat diet had no ill effect on the icterus and kept the children in a better-nourished condition.

---

**The Practical Significance of Uniformly Deep Rectal Temperature Measurements in a Child.**—PAUL TACHAN (*Münch. med. Woch.*, 1912, lix, 2101) conducted 300 double measurements of the rectal temperature in 30 children in an attempt to explain the variations in the rectal temperature so often found in children, without demonstrable cause. Feer had previously indicated that the cause was often found in the variation in the depth to which the thermometer is placed in the rectum, at different times. In each trial the thermometer was inserted only to the end of the mercury bulb and kept there until the mercury remained constant; it was then inserted deeply, about 5 cm., until the mercury remained constant. In this manner ten different measurements were taken on the same child. It was found that between superficial measurement and deep measurement there existed a difference in temperature of between  $0.1^{\circ}$  and  $1.7^{\circ}$  or on an average of  $0.5^{\circ}$ . As a rule, in only a few children did the curve of the superficial reading and the deep reading run quite parallel. More often the temperature difference varied in the same child on different days. Sometimes the superficial curve was very irregular, while the deep curve remained fairly constant. Explanation of the causes of these differences in children was not found. During a fever the difference between the two curves becomes less, but after the temperature has fallen it becomes greater again. Several cases showed an increasingly greater difference after each temperature fall, following a recurring fever, but always approximating again with each new attack of fever. While this investigation may not indicate any new discoveries, it is sufficient to show that in taking rectal temperatures the thermometer should be placed as deeply as possible, and always at the same depth in the rectum.

**The Diagnosis of Tuberculosis of the Lungs in Children.**—HANS VOGT (*Münch. med. Woch.*, 1912, lix, 1957), in this article, selects certain points in tuberculosis of the lung in children which permit of frequent errors in diagnosis. The severe forms of the exudative diathesis have been formerly held to be scrofulous, but Czerny has unmistakably proved that the symptoms of this condition may arise in early infancy, unassociated with tuberculosis, and showing a negative cutaneous tuberculin reaction. Temperature elevation in children where all apparent causes can be eliminated, should not necessarily be put down to a tuberculous infection. In children an increase in temperature occurs frequently over quite a period of time, due to slight infection of the nasopharynx, or even to psychical disturbances. The tuberculin reaction, while a valuable aid in diagnosis, is capable of being misinterpreted. Distinction must be made between an infection by tubercle bacilli and an actual tuberculous process in the body. It is only within very narrow limits that the tuberculous reaction can be applied in a diagnosis of an active process, as in infancy where almost every infection by the bacilli, leads to a progressive tuberculosis. Chronic bronchitis in children is sometimes taken for tuberculosis. From the second to the tenth year Vogt finds as large a proportion of the one as of the other. Especially in case of recurring pneumonia with later areas of circumscribed infiltration and a diffuse bronchitis with occasional exacerbations, is a diagnosis of tuberculosis erroneously made. It rarely occurs that an acute tuberculosis process in the lung will have periods of quiescence, whereas this feature is characteristic of a chronic bronchiectasis.

---

## OBSTETRICS

---

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

---

**The Treatment of Ectopic Gestation.**—CRAGIN (*Surg., Gynec., and Obstet.*, March, 1912) believes that so soon as a diagnosis of unruptured ectopic gestation is positively made, but one method of treatment is permissible—the removal of the pregnant tube by operation. At the time of tubal rupture or abortion, operation is indicated; but some question may arise as to the propriety of operating immediately, or of giving the patient time to recover from shock. Cragin in these cases proceeds as follows: If the patient is seen at the time of a tubal rupture or abortion, operate as soon as careful preparation can be made, unless the patient is in such extreme shock that the operation would probably prove fatal. In this case, watch the patient carefully to see if she is improving or losing ground. If she is improving, operate when the patient is in better condition. If failing, operate rapidly at once, checking hemorrhage with the least manipulation, having an

assistant transfuse, and leaving warm salt solution in the abdomen. Operation should be from above. Two vessels supply the field of operation—the ovarian and uterine—and both should be controlled by a ligature or clamp about the tube, near the uterine cornu and about the upper portion of the infundibulopelvic ligament. The location of these vessels should be kept in mind, and valuable time should not be lost in sponging away blood. The operator should first determine on which side the gestation sac lies, and check hemorrhage as rapidly as possible. As regards the affected tube, it should be removed. If the opposite tube be healthy, this should be allowed to remain. The larger blood clots may be removed by the hands, the smaller may be flushed out by salt solution. The abdomen should be closed without drainage. In interstitial pregnancy, in the majority of cases it is safer to remove the uterus. Occasionally one may excise the affected uterine cornu, leaving the remainder. In intraligamentous rupture and the hemorrhage extraperitoneal and encapsulated, operation may be postponed, with the patient under close observation. Rest in bed, and an ice-bag upon the lower abdomen may check hemorrhage and hasten absorption. If hemorrhage recurs the abdomen should be opened and the source of bleeding controlled. When a pelvic hematoma suppurates, vaginal incision and drainage is the operation of choice. In cases of early ectopic gestation which have ruptured or aborted some time before they are seen, it is usually best to perform abdominal section, removing the tube, blood-clots, and the product of gestation. If suppuration has occurred, vaginal incision and drainage are indicated. In the majority of cases giving a history of tubal pregnancy some time previously, it is best to operate. In a few, where there is no evidence that hemorrhage has recurred, and the tube is empty, and the hematocele diminishing in size, operation may be declined. In advanced ectopic gestation at six months or more, Cragin has operated four times, saving 2 of the children, 1 of whom had congenital dislocation of the hip, but was otherwise healthy. It is best to anticipate spurious labor by operating at eight and one-half months. In dealing with the placenta in these cases, unless the vessels supplying the sac can be ligated and the sac removed entire, the placenta should be left and allowed to separate and come away gradually. Where rupture has occurred downward through the floor of the tube, and the development was intraligamentous, the peritoneum may be raised from the floor of the pelvis and the sac can best be opened by incision at the outer border of the rectus muscle, thus avoiding opening the general peritoneal cavity. The vessels supplying the placenta can often be successfully ligated in these cases, and the sac removed. The abdominal wound may then be closed, and the period of convalescence greatly shortened. Under ordinary circumstances the safest course is to incise the gestation sac, remove the child, stitch the sac to the abdominal wound, and pack the sac with gauze. This should be changed every second or third day, and the separation of the placenta aided with the fingers. The sinus which remains will close in a reasonable time. If the fetus has died some time before operation, and the sac is not infected, the placenta can usually be removed entire. In advanced ectopic gestation, where the fetus has just died, operation may be postponed from four

to six weeks so as to allow the obliteration of bloodvessels. The patient should be under observation, and if evidence of infection occurs, operation should be at once performed. In the presence of infection vaginal section is indicated for drainage; but in the absence of infection the abdominal route is best. If the uterus is found thoroughly adherent to the gestation sac, hysterectomy should be done. In prophylaxis, in cases where it is necessary to remove an ovary, the tube on that side should also be removed, as its presence exposes the patient to the danger of ectopic gestation. In the *Amer. Jour. Obstet.*, April, 1912, JELLINGHAUS reports a case of true, ligamentous, unruptured tubal pregnancy at eight months, treated by abdominal section, with the removal of the gestation sac and placenta and membranes. Five days after operation, vaginal and abdominal fistulæ appeared, and on the tenth day a urinary fistula. At the end of the third week fecal and urinary discharges through the vagina had ceased, but continued through the abdominal opening. This closed by the end of the seventh week. Sixteen weeks after operation the patient felt well, but had watery stools, probably from an intra-abdominal fistula. Markol also reports a case of interstitial pregnancy admitted to hospital five years previously, with what was believed to be an incomplete abortion. Curetting was done but no fetus discovered. The patient left the hospital against advice, returning in a few days in collapse, with rapid pulse and high fever. Her condition precluded operation, but she gradually improved under conservative treatment, and left the hospital. She afterward returned stating that she had been delivered by forceps of a very large child stillborn. Bimanual examination showed a tumor on the right side of the uterus extremely tender, and slightly movable. At operation the tumor was directly connected with the right horn of the uterus. The left tube and ovary were enlarged and bound down by adhesions, and were removed. The appendix and the upper portion of the uterus were also removed. The case was probably one of ruptured ectopic pregnancy, five years previously, with subsequent normal pregnancy, followed by interstitial gestation.

---

**Normal Human Blood Serum in the Disorders of the Newborn.**—WELCH (*Amer. Jour. Obstet.*, April, 1912) reports the case of a premature infant at eight months, taking nourishment badly, and steadily losing weight. Subcutaneous injections of normal human serum, from 20 to 78 c.c., a total of 896 c.c. in twenty-one days, were given with some benefit. The child improved and was able to nurse well. In 32 cases of newborn infants suffering from hemorrhage, this treatment was successful.

---

**Ocular Lesions in the Newborn.**—LEQUEUX (*Archiv. mensuelle l'Obstétrique*, February, 1912), in examining 151 newborn infants found ocular lesions in 37, or 24.5 per cent. These were paralyses, lesions of the cornea, and lesions of the retina. He also observed 1 case of exophthalmos, 1 of nystagmus, 1 of kemosiis, and 1 where there was an abnormal persistence of myelin fibers. The cases of paralysis were those of the seventh pair of cranial nerves, and in 1 case the sixth pair. This followed forceps delivery in difficult labor, with the instru-



ment applied obliquely, one blade over the mastoid region, one over the frontal. Cases where the natural obliquity of the head in labor was lacking comprised the great majority of these. In 2 cases there was paralysis of the seventh and sixth nerves; in 1 the seventh only; in 1 the sixth, and also the roots of the brachial plexus. Lesions of the cornea were most often a cloudiness of varying degree. In some of these cases this disappeared in a short time; in others it persisted for weeks or months. This is usually called traumatic keratitis. It develops in the first twenty-four hours after active labor, often rapidly, and often disappears quickly. In severe cases it may remain. It is usually ascribed to forceps pressure, a blade of the instrument pressing almost directly against the eye. Lequeux found it 6 times, or in 3.9 per cent. of his cases. In 5 of these the lesion disappeared in two or three days; in 1 leukoma resulted; in 3 of the 6 cases forceps were applied, but in 1 of these the instrument was carefully placed over the parietal bones, and direct forceps pressure was absent. Two of the infants were premature. Lequeux believes that this opalescence of the cornea is not infrequent after labor and may readily be overlooked. Direct contusion is not necessary for its production, as the indirect application of force may produce the condition. The pathology of the lesion is obscure and apparently depends upon increase in intra-ocular tension. No treatment is available as most cases recover spontaneously. Retinal lesions were found 15 times, or in 10 per cent. of the cases, most often in both eyes, either at the base of the retina or at other portions. The hemorrhage may extend along the peripheral portion or be circumscribed at the fundus of the retina and choroid. In some cases blood may accumulate between the retina and the vitreus, and may rupture the vitreus. Usually the extravasation is of short duration, leaving minute foci of atrophy in the form of small white dots, which also disappear rapidly. The condition is most often ascribed to contusion and birth pressure in difficult labor with the application of forceps. Lequeux found forceps used in but 12 per cent. of the cases. In breech and shoulder presentations birth pressure is a frequent cause, and the lesion is often accompanied by cerebral hemorrhage or pulmonary apoplexy. It was present in his cases in 14 per cent. of breech extraction; in face presentation the lesion is not infrequent. There seemed to be no difference in the percentage of cases in spontaneous or induced labor, and the accident seemed equally frequent in primiparæ and multiparæ. In 15 cases of contracted pelvis this lesion was present in three infants so born. The weight of the child did not seem to be an essential element, as premature children ill-developed have tissues more liable to hemorrhage than normal infants. There can be no question about the influence of prolonged and difficult labor. Lequeux found an equal proportion of lesions in the anterior and posterior eye. Asphyxia did not seem to be an especially frequent cause of this condition. Blood pressure on the cranium during labor predisposes to this accident. Albuminuria with infarcts in the placenta was also a predisposing cause, and also syphilis. In 6 syphilitic infants, 3 had retinal hemorrhages. Lequeux is impressed with the fact that this condition develops not so frequently from contusion as from intracranial stasis, either papillary stasis from pressure upon the fluid of the cranium and cord, or pressure upon the

venous channels of the cranium and cerebrum. This produces a venous stasis at the border of the retina. Any condition of the blood predisposing to extravasation—as prematurity or syphilis—further the development of this condition. One may find the origin of pigmentation of the retina, which is considered a sign of hereditary syphilis, in these retinal hemorrhages.

---

## GYNECOLOGY

---

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

---

**Vaccine Diagnosis of Gonorrhea.**—STERNBERG (*Gyn. Rundschau*, 1912, vi, 701) says that in treating a large number of cases of inflammatory disease of the uterus and adnexa with gonococcus vaccine, he has found certain clinical manifestations to occur with such regularity in the cases subsequently demonstrated to be of gonorrheal origin that he has come to regard these as of distinct diagnostic value. These manifestations occur usually within a day or two after the first administration of the vaccine, or if this initial dose has been too small, after the next, larger one. They consist, as in practically all forms of immunity reaction, in local, focal, or general disturbances, but in applying gonorrheal vaccine for diagnostic purposes it is desirable as far as possible to avoid local or general reactions, depending upon that at the site of the infection—the focal reaction—to indicate the nature of the condition. For this purpose Sternberg gives an initial dose of 0.3 c.c. of a suspension containing 100,000,000 dead gonococci to the cubic centimeter, injected subcutaneously. If no reaction follows, a few days later a second dose, twice the size of the first, is given. Following this, in gonorrheal cases a marked softening and diminution in tenderness of parametric inflammatory masses and indurated tissue will be noted; the uterus becomes more freely movable, and is much less sensitive to manipulation. If large, tender adnexal masses are present, similar changes occur in these. Sometimes there is a great increase in the amount of discharge, and the next menstrual period may be brought on ahead of time. Increased pain in the pelvic region was complained of only in some cases, and then only for the first day after injection. Control injections of the vaccine have been made on normal individuals, and on those with pelvic masses or indurations of other than gonorrheal origin, without producing any reaction whatever. Especially does this distinction stand out in cases of tubal pregnancy, in which no softening of the mass, or diminution in tenderness, occurs. Sternberg believes, therefore, that this method of diagnosis is of much value, in conjunction with those already in general use.

**Treatment of Injured Ureter by Appendiceal Implantation.**—The suggestion is made by KENNEDY (*Surg., Gyn., and Obstet.*, 1912, xv, 464) that in cases where the ureter has been resected during operation to such an extent that reimplantation into the bladder is not possible, it would be much better to implant it into the vermiform appendix rather than directly into the colon, or than to do an immediate nephrectomy, the methods which heretofore have been most in vogue in treating this condition. He has found by investigations on dogs and on the cadaver that the appendix is practically always sufficiently movable to permit of the right ureter being implanted into its tip or base with ease, and that unless the appendix or meso-appendix is unusually short, it may be brought far enough over to permit of similar treatment of the left ureter. The advantage claimed by Kennedy for this operation over direct implantation into the gut is the relatively cleaner receptacle offered by the appendix, and therefore the reduced chance of ascending infection. The flow of urine through the appendix will prevent its blockage by fecal concretions, and therefore lessen the risk of inflammation in the organ itself. Moreover, the fold of mucosa at its mouth, known as Gerlach's valve, is far more efficient, even in its most imperfect state of development, than any valve action that can be secured artificially, even by oblique insertion of the ureter into the intestinal walls, thus furnishing still further protection against ascending infection. Before attempting to utilize the appendix, however, the permeability of its lumen must be determined with a probe; even if the distal portion were occluded, this could be resected, and the ureter implanted into the stump.

**Normal and Pathological Anatomy of the Endometrium.**—In the four years that have elapsed since the publication of Hitchman and Adler's fundamental work on the cyclic changes occurring in the endometrium, numerous investigators have interested themselves in this subject, and most of them have in a general way confirmed the correctness of the main principles laid down by the above-mentioned authors as to the anatomic conditions of the endometrium during the various phases of the menstrual cycle. Practically all subsequent investigations have shown, however, that marked individual variations from these general principles occur. An attempt to simplify and classify the most important of these variations, as reported by various authors, has been made by SCHRODER (*Arch. f. Gyn.*, 1912, xcvi, 81), who tabulates them as follows: (1) Endometria which show a definite cyclic stage, which, however, does not correspond to the clinical stage. (2) Endometria whose anatomical condition does correspond to the clinical stage, but which show hyperplastic processes, such as invagination or clumping of glands. (3) Endometria which show the anatomic characteristics of several different stages. (4) Endometria which, taken from the ninth to the fourteenth day, show a condition corresponding to the end of menstruation. (5) Endometria which always show one definite gland type, no matter in what period of the menstrual cycle the examination is made. Schröder has examined with great care the endometrium from 205 patients, in all of whom the exact date of the preceding menstruation, and the menstrual type, was known. The specimens were obtained

in part from extirpated uteri, in part by curettage. In 120 of these cases, or 66 per cent., the anatomic picture presented by the endometrium corresponded with the clinical stage at which it was removed; in 22 cases the endometrium presented a uniform anatomic picture, but this corresponded either to an earlier or a later stage than that actually presented by the patient. In all the remaining cases the structure of the endometrium showed variations from the normal, and these have been therefore classed as "pathological" (entirely irrespective of the presence or absence of inflammatory changes). These cases all fall into one of three groups: (1) Endometria which show side by side the characteristics of several stages. (2) Endometria which show diffuse or localized stroma changes without variations in the gland picture. (3) Endometria presenting the picture of glandular or glandular-cystic hyperplasia. Schröder believes that these conditions are all due to disturbances in ovarian function, and has not found any reason to consider inflammatory conditions responsible for them. In the diagnosis of inflammation Schröder depends almost entirely on the round cell and plasma-cell content of the endometrium. He considers a diffuse distribution of round cells throughout the stroma in moderate numbers, and even a moderate amount of grouping of these into small foci, to be a normal occurrence, as is a scattering of plasma cells. As soon, however, as the round cell-groups become larger and more numerous, and the plasma-cell content richer, he considers inflammation to be present, but recognizes that this distinction must be largely subjective. He thinks that no diagnostic value can be placed upon the presence of either edema or hemorrhage, since both may occur purely as the result of operative trauma. The presence of inflammation does not, as a rule, seem to affect the regular cyclic evolution and involution of the endometrium, a point which has been especially brought out by Schröder's investigations being the great persistency in maintaining these cyclic changes exhibited by the endometrium, even in the presence of serious pathological conditions.

---

**Treatment of Incontinence of Urine in Women.**—CASPAR (*Zeitsch. f. Urologie*, 1912, II Beiheft, 238) reports 2 cases of incontinence of urine in women due to stretching or trauma of the urethra and surrounding tissue, in which numerous methods of cure had been tried without success. He was able to produce complete cure in each instance by cauterization of the internal vesical sphincter. The operation is performed through Caspar's operating cystoscope, two or three deep grooves being burned in the sphincter at the point of transit from the bladder to the urethra. This causes scar-formation, and resulting contraction of the sphincter apparatus, which should in most cases be sufficient to produce complete continence, although in some conditions, as for instance, where an extensive prolapse of the anterior vaginal wall is constantly pulling on the sphincter and stretching it, it probably would not be successful. The operation is easy of performance with the proper instrument, and free from danger, and should, Caspar thinks, form a useful addition to our resources in the treatment of what is often an extremely baffling condition. He has also tried it in one case of stubborn enuresis nocturna in a girl, aged sixteen years, likewise with complete success.

## DERMATOLOGY

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

EMERITUS PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

AND

MILTON B. HARTZELL, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

**Some Physiotherapeutic Methods in Dermatology.**—MALCOLM MORRIS (*British Jour. of Derm.*, May, 1912), in an interesting short article gives his experience with some of the newer methods employed in a number of obstinate diseases. His conclusions may be summarized as follows: The  $x$ -rays, radium, Finsen light, and freezing with carbon dioxide snow, are serviceable in the highest degree in early rodent ulcer, in tinea tonsurans, tinea sycosis, and tinea favosa, also in lupus vulgaris and small tuberculous glands, in lupus erythematosus, in certain kinds of nævi, in scars, and in keloid. In these diseases they are superior to medicine, the knife, or to any other form of surgical treatment. They are valuable in a somewhat less degree in later rodent ulcer, and in superficial carcinoma. They are serviceable in varying degrees, in coccogenic sycosis, in hyperidrosis, in hypertrichosis, in chronic eczema, pruritus, and lichenification, and in papilloma, while they possess distinct alleviative influence in such grave affections as Paget's disease, deep-seated carcinoma, sarcoma, mycosis fungoides, and leprosy.

**New Method of Removing Superfluous Hairs.**—W. SCHWENTER-TRACHSLER (*Jour. of Cut. Dis.*, June, 1912, p. 364) refers to 252 cases in which she has employed the following method with success. After removing the entire growth (by shaving ?) the patient rubs pumice stone in twice daily, under which procedure the hair is prevented from coming to the surface, and if this rubbing be persisted in for a year, atrophy of the follicles occurs and finer hairs or no hairs. The skin is never injured by this treatment.

**Treatment of Itching Skin Diseases with Normal Human Serum.**—LINSSEN (*Dermatol. Woch.*, March 30, 1912), quotes a case of impetigo herpetiformis in which a cure followed the injection of serum taken from a normal pregnant woman. This treatment was also employed successfully in other dermatoses associated with pregnancy, and in other itching diseases of the skin, with favorable results, as urticaria, especially in infants, prurigo, and infantile eczema. Good results were obtained in senile pruritus in cases where no benefit had followed saline injections. In generalized eczema in adults favorable results were also obtained. The serum of a healthy pregnant woman is to be used,

that of a non-pregnant woman not proving satisfactory. For females the serum of females and for males that of males should be made use of. The fresher the serum the better. Fifty cubic centimeters of blood are withdrawn from the arm into a sterile centrifugalizing tube containing glass beads, the blood is defibrinated by shaking for five minutes. The serum is separated in the centrifugal machine, sucked up with a sterile syringe, and injected into a vein. In children it is injected subcutaneously. The dose is from 10 to 20 c.c., repeated on successive days, three to five injections being given. The treatment may be used in dispensary practice.

**A Useful Formula for the Widespread Tinea Tonsurans.**—A. W. WILLIAMS (*British Jour. of Derm.*, June, 1912) has used the following formula in a number of cases, and finds it to be remarkably efficacious. It consists of camphor, alcohol, āā ̄iv; picric acid, gr. vii. *Sig.*, Inflammable; paint all over scalp twice daily. An objection to its use is the yellow staining of the hair, which is still noticeable three weeks after stopping the treatment. Camphor and alcohol without the picric acid do not appear to be effective.

**Pemphigus Foliaceus.**—H. H. HAZIN (*Jour. of Cutan. Dis.*, June, 1912) cites a case of this disease in an adult, and also gives the notes of a case of dermatitis exfoliative neonatorum in a child, aged fourteen days, and then discusses the relation of these two diseases, concluding that some cases of pemphigus foliaceus are undoubtedly due to a Bacillus pyocyaneus infection, and that the name dermatitis exfoliativa neonatorum is not a suitable one, as the exfoliation is secondary to a generalized cutaneous infection, probably with the Staphylococcus albus. The two diseases are different, though there may be gradations between them.

**Concerning the So-called Lichen Albus of Zumbusch.**—VIGNOLO-LUTATI (*Dermat. Woch.*, June 8, 1912) gives a case and enters upon the pathological anatomy of the lesions (with microphotographs), and concludes from a study of the literature and his own case, that he is forced to agree with the views already published by Hallopeau, that the affection must be regarded as a type of the sclerous form of lichen of Wilson, and that it is inappropriate to designate it with the new name of "white lichen," which term, moreover, is not exact, since the lesion may be in the beginning, bright red. Under the name of "white spot disease" cases of probably the same disease have been reported of late years by various writers.

**Notice to Contributors.**—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

# INDEX.

## A

AARON, C. D., healing of gastric and duodenal ulcers with bismuth, 495  
 Abnormal fat formation, pathology of, 834  
 Abscess, brain, 153  
     of lung and liver, 597  
 Acetone alcohol in disinfection of hands, 146  
 Aconite, effects of, upon the pulse rate, 788  
 Acne, treatment of, by vaccines, 309  
 Adenocarcinoma of thyroid, 834  
 Adrenalin in pathological sera, 904  
 Albuminuria and cylindruria, 905  
     lordotic, 144  
 Alcoholic heart and liver, 780  
 Alimentary hypersecretion of chronic ulcer as shown by the lactose test meal, 715  
 Amebic dysentery and hepatitis, rapid cure of, 612  
     hypodermic injections of soluble salts of emetin in, 915  
 Ammonia in urine, 600  
 Amyotonia congenita, 732  
 Anaphylaxis, alimentary, 621  
 Anatomy and relations of the tonsil in the hardened body, 37  
 Anders, J. M., stenosis of duodenum, 360  
 Anemia, iron and arsenic in, 451  
 Anesthesia of sciatic nerve, 604  
 Aneurysm of aorta, 754  
 Anthrax, action of salvarsan in, 441  
 Antibodies, comparative study of, 624  
 Antigen reaction of Debré and Parof for rapid diagnosis of urinary tuberculosis, value of, 288  
 Antityphoid vaccination in the army in 1911, 298  
     in the army, results of, 901  
 Antityphoidal immunization by intestinal tract, 155  
 Aortic aneurysm of rheumatic origin, 902  
 Armour, R. G., metastasis of hypernephroma in the nervous system, 726  
 Arneth's leukocytic blood picture in pulmonary tuberculosis, 561  
 Arsenic as a factor in menstruation, 307

Arteries, ulcerations of, 756  
 Articular rheumatism treated by rectal administration of sodium salicylate, 142  
 Arthritis, gonococcic, acute and chronic 369  
     in early life, 469  
 Ascarides, chemistry and toxicology of, 441  
 Ascaris mystax, 131  
 Aseptic serous inflammation upon the dissolution of catgut, 906  
 Asphyxia from descent of excised adenoids in trachea, 775  
 Asthma, calcium salts in treatment of, 295  
     in children, treatment of, 766  
 Atophan in treatment of gout, 911  
 Atropine reaction in cardiac disease, 514  
 Avoidance of anaphylactic phenomena on the injection of immune serum, 289

## B

BACTERIAL endocarditis, 313, 327  
 Bacteriology and pathology of tonsils, 597  
     of peritonitis, 502  
 Baehr, G., glomerular lesions of sub-acute bacterial endocarditis, 327  
 Banti's disease and allied conditions, 856  
 Barringer, T. B., effect of cold air upon the circulation in healthy and sick individuals, 233  
 Basedow's disease, 138  
     experimental production of, 446  
 Bass, M. H., Chvostek's sign and its significance in children, 64  
 Bednar's aphthæ, 145  
 Beebe, S. P., delayed development in a boy treated with thymus gland, 219  
 Bell, A. J., scarlet fever, diphtheria, and measles at Cincinnati contagious hospital, 669  
 Bence-Jones proteinuria, 803  
 Bilirubin in human blood serum, 289  
 Bismuth in gastric and duodenal ulcers, 495

Bismuth poisoning, 647  
 Bladder operations, vaginal route in, 149  
 Blood picture in disease of glands of internal secretion, 598  
   uric acid in, 755  
 Boggs, T. R., Bence-Jones proteinuria, 803  
 Bone formation, production of, 906  
   transplantation of, 291  
 Bowen, J. T., multiple subcutaneous hemangiomas, 189  
 Brachial plexus, supraclavicular anesthesiation of, 604  
 Brain abscess, 153  
   lesions produced by electricity, 541  
 Brannan, J. W., hospital and typhoid carriers, 347  
 Bright's disease, pericarditis in, 286  
 Brown, L., therapeutic use of tuberculin, 524  
 Brown, T. R., studies on the motor functions of the stomach by the use of the gastric and duodenal fistulas, especially as regards the influence of the bitter waters and bitter salts, that is, those containing magnesium sulphate or sodium sulphate, 682  
 Bullous antipyrine eruptions of the buccal cavity, 308  
   eruption associated with appendix abscess, 309

## C

CALCIUM salts in treatment of asthma, 295  
 Callison, J. G., use of vaccines in typhoid fever, 350  
 Camphor and pneumococci, 296  
 Camphorated oil in treatment of pneumonia, 141  
 Cancer at base of skull, 776  
   of larynx, 776  
   of stomach, 754  
   spontaneous cure of, 463  
 Carbohydrate cures in diabetes, 140  
 Carcinoma of rhinopharynx, 153  
   of stomach, 781  
   of tongue, 774  
   of vagina, 151  
   of vulva, 773  
   uteri, control of hemorrhage in radical operation for, 617  
 Cardiac disease, atropine reaction in, 514  
   insufficiency, strophanthin in the treatment of, 143  
   irregularity, the more common forms of, 697  
 Cataract, senile, 466  
 Cesarean section for dystocia, 770  
   repeated classic, 769

Chemistry and toxicology of ascarides, 441  
   of tuberculous sputa, 903  
 Chemotherapy of malignant tumors in experimental animals, 133  
 Chorea minor, treatment of, 299  
   relation of, to rheumatism, 287  
 Chvostek's sign and its significance in children, 64  
 Circle of Willis, function of, 752  
 Claytor, T. A., the more common forms of cardiac irregularity, 697  
 Clitoris, lymphatics of, 306  
 Coagulation time of blood in jaundice, 907  
 Cohen, S. S., non-surgical treatment of exophthalmic goitre, 13  
 Cold air, effect of, upon the circulation in healthy and sick individuals, 233  
 Cole, C. E. C., effects of medicinal doses of aconite upon the pulse rate, 788  
 Coleman, W., weight curves in typhoid fever, 659  
 Collins, J., metastasis of hypernephroma in the nervous system, 726  
 Colloidal selenium A on cancerous glands, 134  
 Complement-fixation test in diagnosis of gonococcus infections of genito-urinary tract, 815  
   in the differential diagnosis of acute and chronic gonococcic arthritis, 369

Constipation, 1  
   and headache in women, 616  
 Cooke, R. A., paroxysmal hemoglobinuria, 203  
 Corbett, J. F., charges in kidney resulting from tying the ureter, 568  
 Cough phenomenon, 600  
 Crotalin treatment of epilepsy, 914  
 Croupous pneumonia, vaccine treatment of, 142  
 Cruice, J. M., incidence of purpura in the course of chronic pulmonary tuberculosis, 875  
 Cryptogamic parasite found in a dermatosis of the type of pityriasis rosea, 508  
 Cryptogenetic granulations of stomach, 707

## D

DAYTON, H., fatal pneumothorax following exploratory puncture, 241  
 Defective development from arthritis in early life, 469  
 Deodorizing excreta, 442  
 Dermatology, physiotherapeutic methods in, 925



Destruction of red blood corpuscles, 154  
 Diabetes, carbohydrate cures in, 140  
     insipidus, 608  
     mellitus and tuberculosis, 543  
 Diarrhea of gastric origin, 170  
 Diastase in urine and feces, 598  
 Digitalis, tincture of, 299  
 Diphtheria carriers, treatment of, by  
     overriding with staphylococcus  
     aureus, 911  
     at Cincinnati contagious hospital,  
     669  
     endotoxin in treatment of diph-  
     theria infection, 607  
     infection, treatment of, 607  
     treatment of, 611  
 Disinfection of drinking water by  
     chlorinated lime, 779  
     of hands by acetone alcohol, 146  
 Dock, G., defective development from  
     arthritis in early life, 469  
 Drug treatment of edema, 8  
 Duodenal ulcers, operation for, 444  
 Duodeno-jejunal occlusion as a sepa-  
     rate condition, 449  
 Duodenum, stenosis of, 360  
     total occlusion of, 770  
     ulcer of, 157  
 Dust-like opacities in vitreous, 467

## E

Ectopic gestation, treatment of, 918  
 Edema, drug treatment of, 8  
 Effects of aconite upon the pulse rate,  
     788  
     of elephantiasis, treatment of, 603  
 Ehrlich's aldehyde reaction in circula-  
     tory diseases, 440  
 Elsberg, C. A., some features of the  
     gross anatomy of the spinal cord  
     and nerve roots, and their bearing  
     on the symptomatology and surgical  
     treatment of spinal disease, 799  
 Emetin salts, hypodermic injections  
     of, 915  
     soluble salts of, 612  
 Emmetropia, size of blind spot and its  
     distance from the point of fixation  
     in, 466  
 End results of fracture of shaft of  
     femur, 606  
 Endocardial lesions of subacute bac-  
     terial endocarditis, 313  
 Endocarditis, acute, treatment of, 452  
     bacterial, 313, 327  
 Endometrium, anatomy of, 923  
 Epidemic of sore throat due to a  
     peculiar streptococcus, 286  
 Epilepsy, crotalin treatment of, 914  
 Ergot, an active principle of, 76  
 Erysipelas, treatment of, 309

Esmarch's tourniquet, paralysis after  
     use of, 292  
 Esophagus, paralysis of, 152  
 Ethmoidectomy for epithelioma, 153  
 Excision of knee, after-treatment of,  
     757, 758, 759  
 Experimental digestive leukocytosis,  
     903  
     eosinophilia after intraperitoneal  
     injection of protein and the  
     relation of eosinophilia to  
     anaphylaxis, 440  
     goitre, non-surgical treatment of,  
     13  
     production of Basedow's disease,  
     138  
 Extirpation of Gasserian ganglion  
     under local anesthesia, 137  
 Eye infirmity, a commentary on the  
     free, 387

## F

FACIAL paralysis following use of  
     nasal douche, 776  
 Facialis phenomenon in later child-  
     hood, 301  
 Farcy of larynx and pharynx, 774  
 Fatal pneumothorax after puncture,  
     241  
 Femur, end results of fracture of shaft  
     of, 606  
 Fetterolf, G., anatomy and relations  
     of the tonsil in the hardened body,  
     37  
 Fever, mechanical production of, 902  
 Fingers, plastic operations on, 907  
 Fishbein, M., bacteriology of peri-  
     tonitis, 502  
 Fistulæ, vesico-intestinal, 909  
 Floating or movable kidney, 753  
 Friedenwald, J., ulcer of stomach and  
     duodenum, 157

## G

Gas poisoning, 577  
 Gasserian ganglion, extirpation of, 137  
 Gastrectomy in multiple carcinoma of  
     stomach, 781  
 Gastric and duodenal ulcers, bismuth  
     in, 495  
     carcinoma, diagnosis of, 291  
     motility, test of, 439  
 Gastroduodenoscopy in affections of  
     stomach and duodenum, 761  
 Gastrointestinal tract, iodine disinfect-  
     ion in, 137  
 Gastroscopy, 776  
 Genital tuberculosis in male, surgical  
     treatment of, 757

- Gibbon, J. H., partial gastrectomy in a case of multiple carcinoma of stomach, 781
- Gittings, J. C., metabolic observations on amyotonia congenita, 732
- Glaucoma, chronic, 466
- Glomerular lesions of subacute bacterial endocarditis, 327
- Glucose, Nylander's test for, 598
- Goitre and cardiac hypertrophy from suspected water sources, 155
- Gonococcal arthritis, acute and chronic, 369
- Gonococcus infections, 815
- Gonorrhea, vaccine diagnosis of, 922
- Gorham, L. W., hemolysis in vivo and in vitro as diagnostic of cancer, 103
- Gout, atophan in treatment of, 911
- Gangrene, phenol, 309
- Graves' disease, congenital, 770
- Gruner, O. C., cryptogenetic granulations of stomach, 707
- Guthrie, C. G., Bence-Jones proteinuria, 803
- H**
- HANDS, plastic operations on, 907
- Hairs, removing superfluous, 925
- Hartzell, M. B., lupus erythematosus and Raynaud's disease, 793
- Hastings, T. W., tuberculin therapy in surgical tuberculosis, 245, 403
- Healing of gastric and duodenal ulcers with bismuth, 495
- Heart, alcoholic, 780
- beat, method of reducing excessive frequency of, 596
- block, 697
- Hemangiomas, multiple subcutaneous, 189
- Hematuria of nephritis and renal papillitis from a surgical standpoint, 293
- Hemoglobinemia and hemoglobinuria, 777
- Hemoglobinuria, paroxysmal, 203
- Hemolysis in vivo and in vitro as diagnostic of cancer, 103
- Hemorrhage of newborn, spontaneous, 297
- Hernia, radical cure of, 447
- Hexamethylenamin in treatment of systemic infections, 913
- use of, in affections of upper respiratory tract, 612
- Histologic changes in myomas and ovaries after the x-rays, 150
- Hormonal, by-effects of, 452, 453
- collapse produced by, 608
- secondary effects of, 451
- Horse flesh in sausages, detection of, 311
- Horse-shoe kidney, hydrarthrosis in a, 446
- surgery of, 445
- Hospitals and typhoid carriers, 347
- Hoyt, D. M., p-hydroxyphenylethylamin, an active principle of ergot, 76
- Human infection with ascaris mystax, 131
- Hunt, E. L., locomotor ataxia, 398
- Hydrarthrosis in a horse-shoe kidney, 446
- Hypertrophied prostate, 756
- Hypertrophy of thymus, surgical treatment of, 136
- I**
- ICTERUS neonatorum, 457
- simplex in childhood, 916
- Illuminating gas poisoning, 577
- Immunity transmission from mother to offspring, 467
- Incidence of purpura in the course of chronic pulmonary tuberculosis, 875
- Incontinence of urine in women, treatment of, 924
- Indicanuria, 827
- Indiscriminate drug taking, 132
- Induction of labor with modified De Ribes bag, 614
- Infant feeding, maltose in, 640
- Infections following tonsillotomy, 30
- Infectious abortion and its relation to man, 619
- Influence of local anemia upon the action of poisons and upon infective processes, 622
- Influenza, pneumococcus, 311
- Inoculation of blood, blood serum, and sperm of syphilitics into rabbits, 285
- Intermittent spiral claudication, 721
- Intestinal poisoning under the guise of a cerebral affection, 765
- Inulin as a foodstuff, value of, 141
- Iodine disinfection in gastro-intestinal tract, 137
- in normal and in syphilitic tissue, distribution of, 778
- in treatment of surgical tuberculosis, 139
- Iron and arsenic in secondary anemia, 451
- Itching skin diseases, treatment of, 259
- J**
- JACKSONIAN epilepsy, 726
- Japanese publication, new, 156
- Jaundice, coagulation time of blood in, 907
- Joint disease, chronic, treatment of, 474
- Juvenile psychasthenia, 865

## K

- KARSNER, H. T., adenocarcinoma of thyroid, 834  
 Keratitis punctata subepitheliasis, 465  
 Kerley, C. G., delayed development in a boy treated with thymus gland, 219  
 Kidney changes following sudden occlusion of ureter, 771  
     resulting from tying the ureter, 568  
     floating or movable, 753  
 Kidneys, formation of arterial capillaries in, 448  
 King, J. M., acute pancreatitis, 221  
 Knee, excision of, after-treatment of, 757, 758, 759  
     tuberculous, excision of, 757, 758, 759  
 Koplik, H., infections following tonsillectomy, 30

## L

- LACTOSE test meal in chronic ulcer, 715  
 Lagrange operation, 466  
 Laparotomy in pneumococcal peritonitis, 286  
 Laryngeal carcinoma of slow evolution, 154  
     paralysis as first symptom of cancer of skull, 776  
 Larynx, cancer of, 776  
 Lawrence, C. H., relation of hypertension to urinary excretion, 330  
 Leukemia, skin changes in, 308  
 Leukocyte and differential counts in ward and open air treatment, 238  
 Leukocytic inclusions in scarlatina, 442  
 Leukocytosis, digestive, 903  
 Lichen albus of Zumbusch, 926  
 Libman, E., endocardial lesions of subacute bacterial endocarditis, 313  
 Lipomas, multiple, 189  
 Lissner, H., hemolysis in vivo and in vitro as diagnostic of cancer, 103  
 Liver, abscess of, 597  
     alcoholic, 780  
     tertiary syphilis of, 625  
 Lobar pneumonia, treatment of, 140  
 Locomotor ataxia, treatment of, 398  
 Lordotic albuminuria, 144  
 Low position of transverse colon, 292  
 Lumbar puncture in treatment of uremia, 763  
 Luminal, a new hypnotic, 761  
     clinical experience with, 763  
 Lung, abscess of, 597  
     malignant disease of, 193  
     ulcerative tuberculosis of, 901  
 Lupus erythematosus, 793  
 Lymphatics of clitoris, 306

## M

- McCARTHY, D. J., adenocarcinoma of thyroid, 834  
 McCombs, R. S., clinical manifestations of illuminating gas poisoning, 577  
 McCrae, T., tertiary syphilis of liver, 625  
 McNeil, A., complement-fixation test in diagnosis of gonococcus infections of genito-urinary tract, 815  
 Magnesium sulphate in treatment of tetanus, 453  
 Malarial pigment and the malarial paroxysm, 904  
 Malignant disease of the lung, 193  
 Maltose in infant feeding, 640  
 Massage in wasting diseases of children, 766  
 Measles at Cincinnati contagious hospital, 669  
     in monkeys, 310  
 Mechanical production of fever, 902  
 Medical education and the midwife problem in the United States, 303  
 Melena neonatorum, normal human blood serum injections in, 295  
     treatment of, 296  
 Meningitis, serous, 915  
 Menstrual fluid, composition of, 306  
 Menstruation, arsenic as a factor in, 307  
 Metabolic observations on amyotonia congenita, 732  
 Metabolism and successful treatment of chronic joint disease, 474  
 Metastasis of hypernephroma in the nervous system, 726  
 Metritis, treatment of, 464  
 Miller, J. L., drug treatment of edema, 8  
 Monkeys, measles in, 309  
 Montgomery, C. H., diabetes mellitus and tuberculosis, 543  
 Morgan, W. G., indicanuria, 827  
 Morse, J. L., maltose in infant feeding, 640  
 Mullaly, E. J., cryptogenetic granulations of stomach, 707  
 Multiple subcutaneous hemangiomas, 189  
 Mumps, 312  
 Myomas and ovaries after x-rays, 150

## N

- NEEDLESS interruption of maternal nursing, 457  
 Neosalvarsan, 452  
     experiences with, 911  
     preliminary report on, 609  
     treatment of syphilis with, 911

- Neosalvarsan on Wassermann reaction, action of, 762
- Neuralgia, trigeminal, 605
- Newmark, L., softening of spinal cord in a syphilitic after an injection of salvarsan, 848
- Nitrogen in urine, 599
- Normal human blood serum in the disorders of newborn, 920
- injections in melena neonatorum, 295
- in treatment of itching skin diseases, 925
- Nutrition and digestion of infants, studies in, 455
- Nylander's test for glucose, 598
- O**
- OCULAR lesions in newborn, 920
- Occult blood in stools and stomach contents, 291
- Orchitis in mumps, local effect of, 312
- Orr, T. G., leukocyte and differential counts in ward and open air treatment, 238
- Orthopedic resection of the pelvis of the kidney for hydrarthrosis, 447
- Osteomyelitis of long bones, 139
- Ovarian pregnancy, 461
- transplantation, 462
- tuberculosis, 150
- Oxyuris vermicularis in appendix, 288
- P**
- PAINTING the peritoneum with tincture of iodine in tuberculous peritonitis, 290
- Pancreatitis, acute, 221
- Paralysis after use of Esmarch's tourniquet, 292
- of esophagus, 152
- of recurrent nerve, 775
- Parasitology of trypanosomiasis, 779
- Paravertebral nerve anesthesia, technique of, 294
- Parenchymatous nephritis, 751
- Parturient and operative cases, early getting up in, 613
- Parturition during adolescence, 458
- Paroxysmal hemoglobinuria, 203
- ventricular tachysystole of psychic origin, 903
- Pasteurization of milk, 753
- Pathological sera, adrenalin in, 904
- Pelvic lymph nodes, surgery of deep, 908
- Pemberton, R., metabolic observations on amyotonia congenita, 732
- Pemberton, R., metabolism and successful treatment of chronic joint disease, 474
- Pemphigus foliaceus, 926
- Perforated stomach, operation for, 444
- Pericarditis in Bright's disease, 286
- Peritoneal tuberculosis, 462
- Peritonitis, bacteriology of, 502
- Pernicious anemia, salvarsan treatment of, 764
- transfusion of blood in, 296
- nausea of pregnancy; diagnosis of, 457
- Pertussis, vaccines in treatment of, 765
- Phenol gangrene, 309
- Phthalein test, 595
- P-hydroxyphenylethylamin, an active principle of ergot, 76
- Pigment, formation of, 310
- Placenta prævia, development of, 613
- Plastic injections, 775
- Pleurisy, sign of, 131
- Plica triangularis, 37
- Pneumococcal peritonitis, laparotomy in, 286
- Pneumococcus infection in man and animals, 776
- influenza, 311
- Pneumonia, camphorated oil in treatment of, 141
- croupous, vaccine treatment of, 142
- experimental, by intrabronchial insufflation, 132
- lobar, 140
- urobilinuria in, 135
- Pneumothorax, fatal, after puncture, 241
- Pregnancy and double pyosalpinx, 460
- differential diagnosis of, 458
- Pressure lowering drugs and therapeutic measures on systolic and diastolic pressure in man, effects of, 449
- Prostate, hypertrophied, 756
- Psychasthenia, juvenile, 865
- Puerperal sepsis, treatment of, by cultures of lactic bacilli, 461
- Pulmonary tuberculosis, chronic, 875
- rest versus climate in treatment of, 535
- treatment of, 142
- Pulse rate, effects of aconite upon, 788
- Punctate keratitis, pathology of superficial, 465
- Purpura in chronic pulmonary tuberculosis, 875
- Pyelotomy in renal calculi, 601
- Pyosalpinx, histology of, 618
- R**
- RADASCH, H. E., brain lesions produced by electricity, 341

Radiologic examination of apices of lungs, 600

Radius, dislocation of head of, 910

Raynaud's disease, 793

Reckord, F. F. D., intermittent-spinal claudication, 721

Rectal temperature measurements in children, 917

Recurrent nerve, paralysis of, 775

Red blood corpuscles, destruction of, 154

Relative value of various substances used as douches, 617

Renal calculi, pyelotomy in, 601  
tuberculosis, origin of, 602

Repeated pregnancy after plastic operations upon the tube, 148

Resection of stomach, Wilms' method of treating the stump in, 909

Rest versus climate in treatment of pulmonary tuberculosis, 535

Retropharyngeal abscess with paralysis of esophagus, 152

Retroversion of gravid uterus with over-distention of bladder, and hematuria, 769

#### Reviews—

Aaron, Diseases of Stomach, 892

Adler, Primary Malignant Growths of the Lungs and Bronchi, 893

Alderson, Dental Anesthetics, 437

Aschoff, Pathologische Anatomie, 276

Bashford, Fourth Scientific Report of the Investigations of the Imperial Cancer Research Fund, 436

Battle, Clinical Lectures on the Acute Abdomen, 437

Benario, Ueber Neuroresidive nach Salvarsan und nach Quecksilberbehandlung, 434

Borruttan, Handbuch der Gesamten Medizinischen Anwendungen der Elektrizität Einschliesslich der Röntgenlehre, 129

Browning, Recent Methods in the Diagnosis and Treatment of Syphilis, 427

Busch, Laboratory Manual of Physiology, 275

Cattell, Lippincott's New Medical Dictionary, 120

Cautley, Diseases of Infants and Children, 431

Chapin, Diseases of Infants and Children, 748

Cheyne, Manual of Surgical Treatment, 739

Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic, Rochester, Minnesota, 117

#### Reviews—

Cornell, Health and Medical Inspection of School Children, 428

Crandon, Surgical After-treatment, 888

Cross and Cole, Modern Microscopy, 899

Cushing, Pituitary Body and its Disorders, 891

Dayton, Practice of Medicine, 890

Donahoe, Manual of Nursing, 130

Douglas, Bacillus of Long Life, 898

Eden, Manual of Gynecology, 121

Einhorn, Diseases of the Stomach, 430

Fischer, Nephritis, 589

Fuchs, Text-book of Ophthalmology, 127

Goodall, Aids to Histology, 750

Grossich, My Method of Preparing the Operative Field with Tincture of Iodine, 895

Hare, Progressive Medicine, 438, 890

Heineman, Laboratory Guide in Bacteriology, 594

Hemmeter, Practical Physiology, 284

Hertzler, Treatise on Tumors, 274

Herz, Disturbances of the Digestive Apparatus, 280

Hunter, Recent Advances in Hematology, 593

Hutchison, An Index of Treatment by Various Writers, 896

Jackson, Diseases of Hair, 885  
Ophthalmic Year Book for 1911, 435

Jardine, Delayed and Complicated Labor, 745

Jessner, Juckende Hautliden, 433

Kollmann and Jacoby, Urologischer Jahresbericht, 900

Köllner, Die Strömungen des Farbensinnes ihre klinische Bedeutung und ihre Diagnose, 747

Lewis, Clinical Disorders of Heart Beat, 744

Lyle, Manual of Physiology, 900

May, Diseases of the Eye, 126

Morton, Principles of Anatomy, 894

Moynihan, Duodenal Ulcer, 271

Niles, Pellagra, 743

Noguchi, Serum Diagnosis of Syphilis, 587

Pels-Leusden, Surgical Operations, 585

Pappenheim, Grundriss der Hamatologischen Diagnostik und Praktischen Blutuntersuchung, 592

Pollock, Gonococcus, 750

## Reviews—

- Roberts, Surgery and Deformities of the Face, 746
- Rogers, Cholera and Its Treatment, 127
- Routh, Cesarean Section in Great Britain and Ireland, 281
- Russell, Preventable Cancer, 749
- Salceby, Surgery and Society, 272
- Salzer, Diagnose und Fehldiagnose von Gehirnerkrankungen aus des Papilla Nervi Optici, 898
- Savage, Ophthalmic Myology, 284
- Scholz, Anomalie Kinder, 130
- Short, New Physiology in Surgical and General Practice, 433
- Simon, Manual of Clinical Diagnosis by Means of Laboratory Methods, 118
- Sudder, Tumors of the Jaws, 429
- Surgical Clinics of John B. Murphy, 118, 889
- Thornton, Pocket Medical Formula, 124
- Turner, Skiagraphy of the Accessory Nasal Sinuses, 897
- Tweedell, Mother's Guide, 283
- Wilson, Handbook of Medical Diagnosis, 125
- Wilson, Practical Lessons in Nursing, 129
- Wood, Pharmacology and Therapeutics, 886
- Ziehen, Die Erkennung der Psychopathischen Konstitutionen, 590
- Rheumatism, relation of chorea to, 287
- sodium salicylate in, 142
- Rheumatoid arthritis, vaccine therapy in, 297
- Rhinopharynx, carcinoma of, 153
- Ringer, P. H., Arneth's leukocytic blood picture in pulmonary tuberculosis, 561
- Roberts, D., alimentary hypersecretion of chronic ulcer as shown by the lactose test meal, 715
- Rochester, De Lancey, constipation, 1
- Röntgen examination and glycyl-tryptophan in diagnosis of cancer of stomach, 754
- Rudolf, R. D., effects of medicinal doses of aconite upon the pulse rate, 788
- Rupture of cranial dura mater in newborn, 768
- of umbilical vessels during labor, 460
- Salvarsan administration of, by mouth to animals and man, 752
- in anthrax, action of, 441
- fever, 142
- in hereditary syphilis, 454
- injection of, 848
- in splenic anemia, 609
- syphilitic nervous disease, 610
- in treatment of scarlet fever, 764
- on Wassermann reaction, action of, 762, 763
- rectal administration of, 135
- relapses, 760
- treatment of pernicious anemia, 764
- Sanatorium and tuberculin treatment of pulmonary tuberculosis, 142
- Sarcoma, 193
- Scarlatina, leukocytic inclusions in, 442
- Scarlet fever at Cincinnati contagious hospital, 669
- infectious period in, 300
- inclusion bodies in blood in, 456
- salvarsan in, 764
- treatment of, 450, 611
- Schwartz, H. J., complement-fixation test in diagnosis of gonococcus infection of genito-urinary tract, 815
- in the differential diagnosis of acute and chronic gonococcic arthritis, 369
- Sciatic nerve, anesthesia of, 604
- Sclerectomy with iridectomy in chronic glaucoma, 466
- Selenium A, 134
- Sepsis in newborn originating in Bednar's aphthæ, 145
- Serofibrinous pleurisy, 131
- Serous meningitis, 915
- Sigmoid and rectum, extensive resection of, 602
- Sinusitis, frontal, 775
- Skin changes in leukemias, 308
- Smithies, F., trichomonas hominis in gastric contents, 82
- Sodium salicylate in acute articular rheumatism, 142
- Softening of spinal cord after salvarsan, 848
- Spastic bronchitis, acute, treatment of, 454
- Spitzka, E. A., brain lesions produced by electricity, 341
- Spinal disease, surgical treatment of, 799
- Splenic anemia treated with salvarsan, 609
- Sputa, tuberculous, 903
- Stein, R., Banti's disease and allied conditions, 850

## S

- Sacro-iliac displacement, 94
- Salvarsan and sublimate, 778

Stenoses, nasal, 775  
 of duodenum, 360  
 Stevens, A. A., malignant disease of the lung, 193  
 Stomach, carcinoma of, 781  
 and duodenum, surgical pathology of, 447  
 cancer of, 754  
 cryptogenetic granulations of, 707  
 diagnosis of surgical conditions of, 291  
 studies on motor functions of, 682  
 ulcer of, 157  
 Strabismus operations, failure in, 466  
 Striae of pregnancy, prevention of formation of, 302  
 Strophanthin in treatment of cardiac insufficiency, 143  
 Sugar in blood in pregnancy, 458  
 Summer heat on infants and children, effect of, 143  
 Suprasympyseal Cesarean section, 613  
 Surgery of horse-shoe kidney, 445  
 Surgical tuberculosis, tuberculin therapy in, 245, 403  
 Sutton, R. L., clinical note on verrucae plantares, 71  
 Symphysis and other pelvic joints in parturient patients, changes in, 459  
 Syphilis, hereditary, salvarsan in, 454  
 of liver, 625  
 Syphilitic affections of bones in childhood, 145

## T

TABES, causes of death in, 287  
 Talley, J. E., atropine reaction in cardiac disease, 514  
 Tertiary syphilis of liver, 625  
 Tetanus, treatment of, 453  
 Theophyllin on nitrogenous excretion, influence of, 609  
 Thymus gland, delayed development in a boy treated with, 219  
 hypertrophy of, 136  
 Tinea capitis, 309  
 tonsurans, useful formula for, 926  
 Tongue, carcinoma, 774  
 Tonsil enucleation, principles and practice of, 37  
 Tonsillotomy, infections following, 30  
 Tonsils, bacteriology and pathology of, 597  
 Transfusion of blood in pernicious anemia, 296  
 Transplantation of bone, 291  
 Transverse colon, low position of, 292  
 Trauma, as a factor in rupture of pyosalpinx, 773  
 Treponema pallidum as the causative agent of syphilis, establishment of, 443

Trichiniasis, 312  
 Trichocephalus trichiura in appendix, 288  
 Trichomonas hominis in gastric contents, 82  
 Trigeminal neuralgia, treatment for, 605  
 Tubal pregnancy, cause of rupture in, 302  
 Tuberculin, therapeutic use of, 524  
 therapy in surgical tuberculosis, 245, 403  
 treatment of tuberculosis, 142  
 Tuberculosis, 245, 403, 543, 561  
 apical lesion in, 468  
 epidemiology of, 623  
 genital, in male, 757  
 iodine in treatment of, 139  
 of lung, ulcerative, 901  
 of lungs in children, diagnosis of, 918  
 ovarian, 150  
 pulmonary, treatment of, 535  
 renal, 602  
 source and development of generalized, 156  
 urinary, diagnosis of, 288  
 Tuberculous knee, excision of, 758  
 peritonitis, painting the peritoneum with tincture of iodine in, 290  
 sputa, chemistry of, 903  
 Typhoid carriers, 347  
 fever, high calory diet in, 610  
 in infancy, 767  
 serum treatment of, 452  
 use of vaccines in, 350  
 weight curves in, 659  
 stools, new anaërobic bacillus in, 311  
 vaccination for, 912  
 Typhoidal bacteriemia with localization in the lung, 155  
 Tyramine, 76

## U

ULCER of stomach and duodenum, 157  
 Ulcerations of arteries, 756  
 Ulcerative tuberculosis of lung, 901  
 Ulna, fracture of, 910  
 Urea in urine, determination of, 290  
 Uremia, treatment of, 763  
 Ureter, changes in kidney resulting from tying, 568  
 occlusion of, 771  
 treatment of, by appendiceal implantation, 923  
 Uric acid in blood, determination of, 755  
 Urinary excretion, relation of hypertension to, 330  
 tuberculosis, diagnosis of, 288  
 Urine, ammonia in, 600

Urine and feces, diastase in, 598  
 incontinence of, 924  
 nitrogen in, 599  
 Urobilin in human blood serum, 289  
 Urobilinuria in pneumonia, 135  
 Uterine scar after Cesarean section, 768

## V

VACCINATION with sensitized agents, 622  
 for typhoid by living sensibilized bacilli typhosi, 912  
 Vaccine, diagnosis of gonorrhea, 922  
 in treatment of acne, 309  
 of croupous pneumonia, 142  
 of pertussis, 765  
 therapy in rheumatoid arthritis, 297  
 use of, in typhoid fever, 350  
 Vagina, carcinoma of, 151  
 Vaginal hysterectomy under local anesthesia, 305  
 route in bladder operations, 149  
 VanderHoof, D., diarrhea of gastric origin, 170  
 Varix involving soft palate, left tonsil, and pharyngeal wall, 152  
 Verruæ plantares, clinical note on, 71  
 Vesico-intestinal fistulæ, study of, 909  
 Vital staining, process of, 623  
 Vitreous, dust-like opacities in, 467  
 Volkmann's ischemic paralysis, treatment of, 601

Voorsanger, W. C., rest versus climate in treatment of pulmonary tuberculosis, 535  
 Vulva, carcinoma of, 773

## W

WARFIELD, L. M., bismuth poisoning, 647  
 Wassermann reaction with or without treatment by salvarsan, 147  
 Weight curves in typhoid fever, 659  
 Williams, T. A., juvenile psychasthenia, 865  
 Wilms method of treating the stump in resection of stomach, 909  
 Würdemann, H. V., commentary on the free eye infirmary, 386

## X

X-RAY treatment of gynecological skin affections, 616

## Y

YOUNG, J. K., sacro-iliac displacement, 94

## Z

ZUMBUSCH, so-called lichen albus of, 926

